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Original Communications

DIAGNOSIS AND MANAGEMENT OF SEVERE INFECTIONS IN INFANTS AND CHILDREN: A REVIEW OF EXPERIENCES SINCE THE INTRODUCTION OF SULFONAMIDE THERAPY

III. MENINGOCOCCAL INFECTIONS

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A. EXPERIENCES AT THE ST. LOUIS CHILDREN'S HOSPITAL

THIS paper presents an analysis of our experiences in managing meningococcal infections in 77 children at the St. Louis Children's Hospital since the advent of sulfonamide chemotherapy. The years 1937-1942 represent nonepidemic years during which time only a small number of cases with meningococcal infections were admitted. The years 1943-1944 represent the greatest epidemic years in this country's history.[1] The majority of the cases in this series was seen during these last two years. The contagious pavilion at the St. Louis Children's Hospital can accommodate comparatively few patients, and so most of the patients with meningococcal infections were sent to the St. Louis Isolation Hospital. A review of these cases will appear in the second half of this paper.

ANALYSIS OF DATA

A. DISTRIBUTION OF PATIENTS BETWEEN 1937 AND 1944.—The incidence of meningococcal infections between the years 1937 and 1942 was

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CHART I

DISTRIBUTION OF PATIENTS 1937 TO 1944 DURING MONTHS OF EACH YEAR

YEAR	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	TOTAL PATIENTS
1937	2				2	1				1		1	7
1938	2	1	1		1						2		7
1939	1			1									2
1940											1	1	2
1941		1		1			1						3
1942				2	1						1	3	7
1943	2	3	3	2	1	2	1	1	1	1	1	5	23
1944	9	7	8	2									26
YEAR	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	TOTAL PATIENTS

Chart I.—Monthly and yearly incidence of cases of meningococcal infections seen at the St. Louis Children's Hospital over the period 1937-1944.

sporadic and low, from two to seven per year (Chart I). If we examine the number of cases in the year of 1943, we see that every month of the year contributed at least one patient. The first six months and the last month of the year contributed most of the patients. In 1944, the first few months of the year also contributed most of the patients. This predilection for the first six months of the year is even more definitely illustrated by the Isolation Hospital material.

B. SEX DISTRIBUTION OF CASES.—There was a definite preponderance of males, 50 as compared to 27 females, although this was not true at the Isolation Hospital.

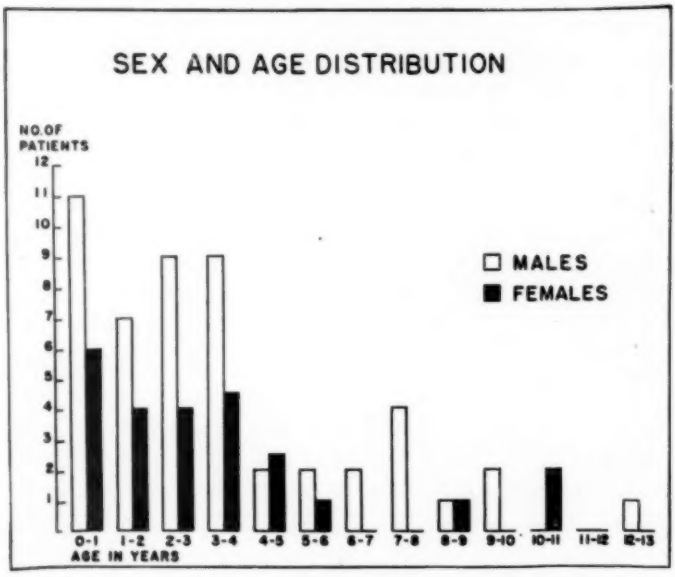

Chart II.—Age and sex distribution of cases of meningococcal infections seen at the St. Louis Children's Hospital over the period 1937-1944.

C. Age Distribution.—The disease seems to have a greater preference in both sexes for the first few years of life (Chart II).

D. Day of Disease When Therapy Was Instituted.—Probably the most important deciding factor in the favorable outcome of a meningococcal infection is the institution of adequate sulfonamide chemotherapy very early in the disease. The following is a table which illustrates the distribution of patients with relation to the apparent day of the disease when therapy was instituted.

DAYS ELAPSING BEFORE TREATMENT	NUMBER OF PATIENTS
0 to 1	4
1	28
2	11
3	12
4	7
5	4
6	1
7	2
8	0
9	1
2 weeks	2
3 weeks	3

Thirty-two patients entered the hospital after three days of illness and five patients after two weeks.

Only six patients received some sort of sulfonamide therapy before entry into the hospital, and in most instances this therapy was inadequate.

E. Criterion for Diagnosis.—All cases included in this series are proved cases of meningococcal infections in that the meningococcus was cultured either from the blood stream or spinal fluid of each patient.

F. Symptoms and Signs.—The following symptoms were noted:

SYMPTOMS	NUMBER OF PATIENTS
Fever	73
Headache	18
Lethargy	56
Vomiting	60
Sore throat	4
Malaise	26
Convulsions	12

As we can see from the foregoing table, fever, lethargy, and vomiting were the most frequent symptoms.

The following signs were seen:

SIGNS	NUMBER OF PATIENTS
Petechiae	47
Stiff neck	66
Positive Kernig and Brudzinski signs	61
Collapse	9

A petechial eruption was seen in approximately three-quarters of all the patients and was a very important sign in helping to establish a diagnosis of meningococcal infection. In approximately one-fourth of the cases, however, it was absent. Frequently stained smears of serum

from the cut surface of a purpuric lesion revealed gram-negative diplococci.

G. VARIETIES OF MENINGOCOCCAL INFECTIONS.—

1. *Meningococcemia Without Meningitis.*—Ten such cases were seen. In all, lumbar punctures were performed, and the cell counts were within normal limits, and the cultures were sterile. Three of these cases (T-261, 0-2269, N-914) were what must be classified as fulminating; that is, they were marked by an abrupt onset of symptoms, profound toxemia, and profuse purpuric rash, and all terminated in death in a few hours. The other 7 cases were mild in that the patients did not seem very ill and made uneventful recoveries after a course of sulfonamide chemotherapy.

2. *Meningococcemia and Meningitis.*—This group was represented by 9 patients. All of these patients recovered.

3. *Meningitis Without Meningococcemia.*—There were 58 patients in this group. In not all cases was the spinal fluid purulent. In 4 cases the spinal fluid cell count ranged from 10 to 800 with polymorphonuclear cells predominating. Most of these patients had a very mild course as illustrated by Chart III while a few had very hectic ones as illustrated by Chart IV.

H. LABORATORY DATA.—Our laboratory employed two techniques in isolating the meningococcus from spinal fluid and block. One was the usual laboratory method, employing tubes of blood agar* slants (for spinal fluid cultures) from which most of the air was exhausted by means of a water vacuum pump. The blood of the patients was cultured in tryptose broth.†

The other technique involved the use of the chorioallantoic membrane of the chick embryo as described by Blattner, Heys, and Hartmann.[2] This technique proved to be a valuable adjunct to the usual laboratory facilities for isolating organisms from body fluids of patients, especially after a patient was receiving sulfonamide chemotherapy. This point is emphasized in the foregoing reference.

In analyzing our results we were able to culture the meningococcus from the spinal fluids of 66 patients in 8 of which positive cultures were obtained only by the chick embryo method. Organisms were seen in the stained smears of the spinal fluids of only 53 patients. As recounted previously, meningococci were cultured from the blood stream in only 19 patients. In 10 cases, however, no blood cultures were made.

I. THERAPY.—

1. *Serum.*—This therapy was used in 12 patients. It is difficult to make a statement about the efficacy of serum therapy, but our impression is that serum does not enhance the effectiveness of chemotherapy. This

*Blood agar—composition: Distilled water, bacto-tryptose 2 per cent, NaCl 0.5 per cent, Na_2HPO_4 0.3 per cent, para-aminobenzoic acid 5 mg. per cent, defibrinated rabbit blood 5 per cent.

†Above composition but lacking in agar and defibrinated blood.

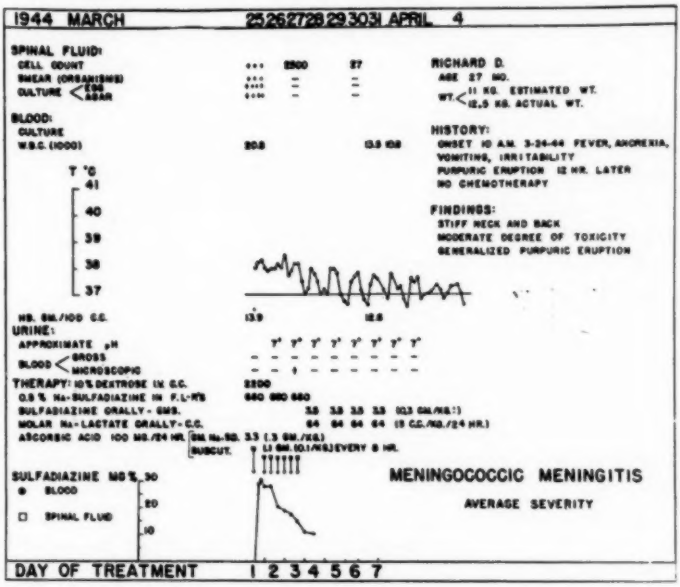

Chart III.—Clinical course of a case of meningococcal meningitis of "average" severity.

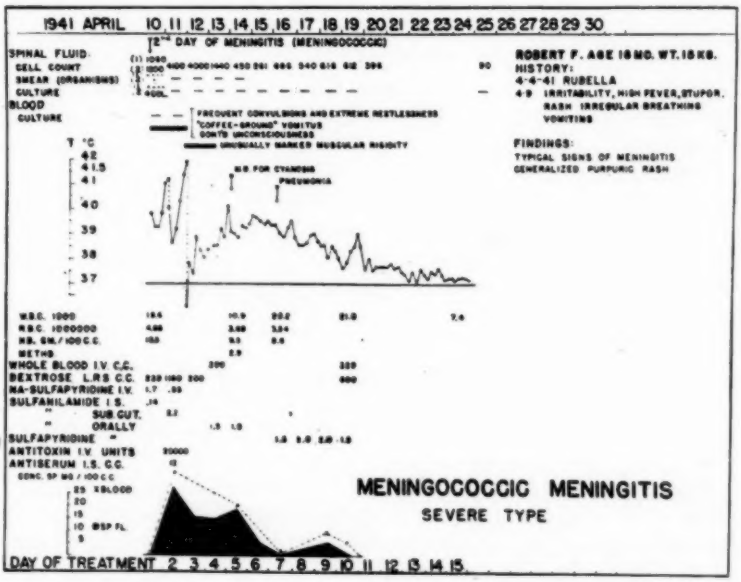

Chart IV.—Clinical course of a very severe type of meningococcal meningitis.

was also our impression after we studied our larger series of cases from the St. Louis Isolation Hospital. In what appeared to be overwhelming infections, we hesitated, however, to withhold serum therapy.

2. *Sulfonamide Chemotherapy.*—Six sulfonamide drugs were used: prontysil (4′ sulfonamido-2, 4-diaminobenzene), sulfanilamide (*p*-aminobenzene sulfonamide), sulfapyridine (2-*p*-sulfanilamidopyridine), sulfadiazine (2-*p*-aminobenzene sulfonamidopyrimidine), sulfapyrazine (2-sulfanilamidopyrazine), and sulfamerazine (2-sulfanilamido-4-methylpyrimidine).

The number of patients treated with each drug was:

Prontysil	1 patient
Sulfanilamide	5 patients
Sulfapyridine	5 patients
Sulfadiazine	33 patients
Sulfapyrazine	9 patients
Sulfamerazine	14 patients

There were a few patients who were treated with two drugs because they developed urinary complications and had to be placed upon sulfanilamide.

There was some variation in the therapy of these 77 patients. Three routes of drug administration were employed; that is, intrathecal, intravenous, and oral. It was not until 1942 that our present therapy for meningococcal infections became more or less routine and we formulated certain principles. These were:

(a) It was definitely decided that intensive sulfonamide chemotherapy was the treatment of choice. For the first twenty-four to forty-eight hours the patients received 0.6 Gm. per kilogram of body weight per day of sulfonamide. The reason for this was that many times the responsible organism was not isolated for from twenty-four to forty-eight hours, so that we were in doubt during that interval as to the kind of purulent meningitis with which we were dealing. It was because of such a possibility that we felt that the patients should be treated at the outset in a way that would be adequate for such more serious infections as pneumococcal or influenzal meningitis. By employing this type of therapy, valuable time was not lost in a case which was thought at first to be a meningococcus meningitis and after from two to three days was found to be a more serious type.

The drug was administered parenterally for the first twenty-four to forty-eight hours (0.6 Gm. per kilogram of body weight per day), and as soon as the meningococcus was isolated either from the spinal fluid or blood of a patient, the dose of the sulfonamide drug was reduced to 0.3 Gm. per kilogram of body weight per day, provided that reduction of dosage also seemed justified by clinical improvement of the patient. This latter dosage was continued until the temperature remained normal for two days. It was then reduced to 0.2 Gm. per kilogram of body weight per day. After two more days of normal temperature, the dose was cut to 0.1 Gm. per kilogram of body weight per day, and after two

days more of normal temperature chemotherapy was discontinued. If the patients remained afebrile for from two to three days after the discontinuation of chemotherapy, they were discharged. The average duration of chemotherapy was 10.6 days; the average hospital stay was 14.1 days.

(b) Parenteral chemotherapy for the first day or two was selected because most of our patients were comatose, irrational, uncooperative, or vomiting upon admission, so that oral administration of the sulfonamide drug was either impossible or unreliable.

(c) In January, 1943, the subcutaneous route of drug administration was adopted as the route of choice. This decision was primarily the result of the work of Barnett and associates,[3] who noted that the speed in attaining a desired sustained drug level in the blood was almost as rapid by the subcutaneous as by the intravenous route, the plateau being reached from below upward. Theoretically the risk of precipitation in the urinary tract would be less in this way than by the intravenous route.

(d) About the same time, it was appreciated that the alkalinization of the urine was of great value in reducing the degree of crystalluria in the case of certain of the drugs. It was found by giving 12 adults and a group of more than 50 children 5 c.c. per kilogram of body weight per day of molar sodium lactate in four divided doses the urine would be rendered alkaline (pH 7 to 8). The sulfonamide drugs in 0.5 per cent solution were, therefore, incorporated in a mixture of one-half "fortified lactate Ringer's."* The following dosage regimes have been adapted for sulfadiazine and sulfamerazine for the first twenty-four to forty-eight hours.

Sulfadiazine: 60 c.c. per kilogram of body weight of a 0.5 per cent solution of sodium sulfadiazine (0.3 Gm. per kilogram) made up in one-half "fortified lactate Ringer's" solution for the initial dose and 30 c.c. per kilogram of body weight of the above solution (0.15 Gm. per kilogram) every eight hours for the first twenty-four to forty-eight hours.

Sulfamerazine: After an initial dose similar to that of sulfadiazine, 20 c.c. per kilogram of body weight (0.1 Gm. per kilogram) of the solution were given every eight hours for the first twenty-four to forty-eight hours.

When the patient was able to take drug by mouth, the lactate was given in fruit juice or milk formula. The amount given was 5 c.c. per kilogram of body weight of a molar solution in four divided doses during the twenty-four hours.

This form of drug administration accomplishes the following:

(1) The subcutaneous route of drug administration is extremely easy from a technical viewpoint and is especially valuable in pediatrics.

*Half fortified lactate Ringer's: Sodium lactate made up to 1/20 molar in Ringer's solution.

(2) An adequate sulfonamide blood level is rapidly attained in from one to three hours.[3] It is often difficult to obtain the desired high levels of drug by oral dosage.

(3) Hydration is necessarily accomplished by the large amount of fluid in which the 0.5 per cent drug is given, and it becomes automatically impossible to create dangerously high drug levels because of unrelieved dehydration.

(4) Any chloride deficit caused by vomiting is replaced by the Ringer's salts and renders more certain the prompt secretion of an alkaline urine, which is made possible because of the added sodium lactate. In addition to the alkalinizing effect of the sodium lactate, the glucogenic effect of this substance was also desirable. Another advantage to the use of sodium lactate is that it is very easily adaptable to oral as well as parenteral use and when given orally does not have the undesirable effect of sodium bicarbonate in causing belching, vomiting, and in reducing too much the acidity of the gastric juice.

J. Other Adjuncts of Therapy.—

(1) Adequate hydration was keenly stressed, and all patients were given in a minimum of 10 per cent of their body weight in fluids per day.

(2) Careful charts were kept of each patient's daily intake and output.

(3) Urine examinations were made daily. The pH of the urine was determined with nitrazine paper, and the urine was tested for albumin, and the microscopic sediment was examined for cellular elements.

(4) A white blood cell count was made every other day.

(5) Blood cultures were obtained upon admission and at any time when there occurred a sudden spike in temperature to 39° C. or over.

(6) A lumbar puncture was performed upon all patients on admission and was usually repeated every three to four days if fever persisted and again shortly before each patient was discharged from the hospital. All spinal fluids were examined for cellular elements and cultured either on blood agar or upon the chorioallantoic membrane of the chick embryo.

(7) Sulfonamide drug levels were obtained every day for the first three hospital days and usually every other day thereafter.

K. Complications From Drug.—

COMPLICATIONS	NUMBER OF PATIENTS	
Hematuria		
Gross	9	11.6%
Microscopic	5	6.4%
Fever	2	2.3%
Rash	1	1.2%
Cyanosis	14	18.1%

The most frequent complication we saw was cyanosis. This was due to methemoglobin formation—all in patients who were treated with sulfanilamide. Whenever thought necessary, methemoglobinemia was controlled by appropriate dosage of methylene blue.[4]

The 9 cases of gross hematuria were made up of 8 patients who received sulfadiazine and 1 who received sulfapyrazine. The other toxic complications were of little importance.

It must be remembered that the patients in this series received intensive sulfonamide chemotherapy (see range of drug levels in Table I), and the 9 cases of gross hematuria must be interpreted with that in mind. In all instances the hematuria subsided promptly as soon as the intensive chemotherapy was relaxed or the offending drug discontinued entirely.

L. Complications From the Disease.—

COMPLICATIONS	NUMBER OF PATIENTS	
Arthritis	8	10.3%
Deafness	5	6.4%
Encephalitis	2	2.3%
Paralysis	6	7.7%

Arthritis was the most frequent complication seen and usually involved multiple joints of the body. It usually appeared during convalescence and was never very severe, the joints being tender for a few days, showing fusiform swelling, and usually subsiding spontaneously.

Paralysis was the next most frequent complication and usually involved the extraocular muscles. Strabismus so produced appeared both early and late in the disease and subsided spontaneously in all cases. Only one case of hemiparesis was seen, and this cleared up by the time of the patient's discharge from the hospital.

Deafness was encountered in only 6.4 per cent of the cases. This was usually noted during convalescence and was of the nerve type, usually involving both ears, and seemed permanent.

The last and rather infrequent complication was a postinfectious type of encaphalitis which was characterized by behavior changes and emotional instability. In both cases which have been followed since dismissal from the hospital there has been a definite but slow recovery.

M. Mortality Rate.—Eleven of the 77 patients (14.2 per cent) expired. If we analyze these deaths (Table II), we see that the patient, S-3067, died as a result of bronchiolitis well after the meningitic process had subsided. Three patients expired before any form of therapy could be instituted, and 7 patients died during the first twenty hours in the hospital, and only 3 patients expired who received the full dosage of chemotherapy, 3.8 per cent of the total number. Not one received any sulfonamide drug before admission to the hospital.

N. Autopsy Reports.—We were able to perform post-mortem examinations on 7 out of the 11 patients who expired. We see (Table II)

TABLE

CASE	DATE OF ADMISSION	HISTORY NO.	SEX	AGE	BODY WT. (KG.)	APPARENT DAY OF MENINGITIS WHEN THERAPY WAS BEGUN	SULFONAMIDE				
							DRUG USED	TOTAL GM.	ROUTE ADMINISTERED		
									IV	SC	IT	ORAL
1	1/28/37	N-231	F	2⅔ yr.	?	4 days	0					
2	1/28/37	K-2664	F	5 yr.	?	2 days	0					
3	5/ 2/37	N-711	M	1½ yr.	12.2	5 days	Prontylin	24.6		4.6	1.0	18.96
4	5/ 9/37	N-748	M	6 mo.	?	26 days						
5	6/ 3/37	N-906	M	3½ yr.	11.1	1½ days	SA	15.2	0	13.9	1.3	6.4
							PR	6.4				
6	10/24/37	N-1943	M	5 mo.	11.0	2 days	0					
7	12/30/37	N-2289	M	8 yr.	22.3	1 wk.	SA	27.7	0	17.0	1.03	9.7
8	1/18/38	N-914	M	6 yr.	22.2	1 day	SA	5	0	5	0	0
9	1/18/38	N-111	F	5 yr.	19.5	4 days	SA	96.9	0	22.0	1.54	73.4
10	2/19/38	O-413	F	1½ yr.	9.6	2 wk.	SA	11.1	0	10.0	1.1	0
11	3/ 8/38	O-507	M	1½ yr.	11.0	3 days	SA	25.1	0	6	1.1	18.0
12	5/ 1/38	O-869	M	6 mo.	7.2	2 wk.	SA	11.4	0	4.5	1.7	5.2
13	11/ 1/38	O-2240	M	4 yr.	20.0	3 days	SA	49.4	0	30.5	.73	18.2
14	11/ 5/38	O-2269	M	2½ yr.	18.0	1 day	SA	2.0	0	2.0	0	0
15	1/19/39	P-210	F	6 mo.	11.5	4 days	SP	5.5	0	0	0	5.5
16	4/14/39	P-783	M	1 mo.	3.3	1 wk.	SA	8.1	0	0	.1	7.95
							SP	.9	0	0	0	.9
17	11/21/40	Q-2485	M	4 yr.	15.9	1 day	SP	1.5	1.5	0	0	0
18	12/15/40	Q-2296	M	3 mo.	4.2	1 day	SP	27.4	.4	0	.15	26.8
							SA	.42	.42	0	0	0
19	2/ 5/41	R-301	M	3 yr.	15.0	1 day	SP	8.9	2.2	0	0	6.7
20	4/10/41	R-703	M	16 mo.	11.1	5 days	SA	5.1	0	2.2	.26	2.6
							SP	10.1	1.6	0	0	8.5
21	7/20/41	R-1511	M	6 wk.	5.2	½ day	SA	19.0	0	0	0	19.0
							SP	2.1	1.1	0	0	0
22	4/ 6/42	S-748	M	9 mo.	9.0	6 days	SD	61.9	3.9	0	0	58.0
23	4/22/42	S-878	M	10 yr.	25.0	2 days	SD	79	5	0	0	74
24	5/29/42	S-1173	M	4 yr.	30.0	5 days	SD	8	0	0	0	8
25	11/27/42	S-2914	M	2 yr.	11.0	2 days	SD	87	9.7	.4	0	77
26	12/ 4/42	S-2951	F	11 mo.	7.9	3 wk.	SD	5.0	4.8	.2	0	0
27	12/14/42	S-3018	M	17 mo.	9.5	4 days	SD	29.2	5	.26	0	24
28	12/22/42	S-3067	M	2 yr.	12.7	1 day	SD	40.5	6.25	0	0	34.3
29	1/ 4/43	T-120	F	10 mo.	7.2	5 days	SD	38.5	5.0	0	0	33.5
30	1/24/43	T-261	M	4 mo.	?	1 day	0					
31	2/17/43	T-454	M	3 yr.	15.4	1 day	SD	35.9	0	0	2.85	33
32	2/24/43	T-191	M	7 yr.	26.3	36 hr.	SD	4.6	0	0	2.6	2
							SA	75.0			3.0	72
33	2/26/43	T-530	F	6 yr.	21.3	2 days	SD	67.6	0	0	8.8	58.8
34	3/ 6/43	T-581	F	11 yr.	50.0	2 days	SPZ	37.5	0	0	15.5	32.0
35	3/10/43	T-611	F	15 mo.	9.2	1 day	SPZ	35	0	9.0	0	26
36	3/21/43	T-695	F	9 yr.	26.0	?	SPZ	79.0	0	0	13	66
37	4/ 2/43	T-799	F	2 yr.	9.1	2 days	SD	66.5	0	0	8.5	58.0
38	4/16/43	T-927	M	2½ yr.	11.3	2 days	SPZ	17.7	0	0	17.7	0
39	5/31/43	T-987	F	5 yr.	21.8	1 day	SD	6.8	0	0	6.8	0
							SA	10.4			4.4	6
							SPZ	38.2			2.2	36
40	6/16/43	T-1477	M	11 mo.	8.6	2 days	SD	40.5	0	0	10.5	30
41	6/22/43	T-1528	F	2 yr.	7.7	3 days	SD	24.75	0	0	4.75	20
42	7/ 2/43	T-1650	M	10 yr.	40.0	3 days	SD	58.0	0	0	18.0	40
43	8/15/43	T-2053	F	5 yr.	14.5	3 days	SPZ	54.0	0	0	16.5	37.5
44	9/23/43	T-2400	M	7 yr.	28.1	1 day	SPZ	109.5	0	0	22.5	87.0
45	10/10/43	R-1578	M	2½ yr.	11.3	1 day	SPZ	45.9	0	0	13.5	32.4
46	11/18/43	T-2836	F	6 mo.	7.4	12 hr.	SPZ	14.3	0	5.3	0	9.0
47	12/ 6/43	T-2949	M	15 mo.	12.9	36 hr.	SD	40.75	0	0	13.25	27.5
48	12/ 5/43	T-2994	M	3 yr.	15.0	3 days	SD	21.0	0	0	3.0	18.0
49	12/18/43	T-3000	M	6 yr.	27.2	4 days	SM	24.0	0	0	4.5	19.5
50	12/18/43	T-3003	F	11 yr.	31.3	1 day	SM	23.7	0	0	9.4	14.25
51	12/31/43	T-3058	M	2½ yr.	12.2	2 days	SD	55.7	0	0	7.7	48.0
52	1/ 2/44	U-106	M	2½ yr.	12.0	9 days	SD	33.6	0	0	33.6	0
53	1/ 5/44	U-121	M	8 yr.	20.0	3 days	SM	27.5	0	0	14.0	12.0

*SA = Sulfanilamide; ST = Sulfathiazole; SP = Sulfapyridine; SPZ = Sulfapyrazine; SM = Sulfamerazine; SD = Sulfadiazine; PR = Prontosil; AT = Antitoxin; S = Serum; S.F. = Spinal Fluid.

THERAPY*					BACTERIOLOGICAL DATA							
TOTAL NO. OF DAYS ON DRUG	CONCENTRATION MG./100 C.C.			SERUM THERAPY	SP. FLUID SMEAR		CULTURE		BLOOD CULTURE	OUTCOME	DAYS IN HOSP.	THERAPY BEFORE ENTRY
	2ND DAY	3RD DAY	4TH DAY		CELLS	ORG.	EGG	BL. AGAR				
				AT+S	8,500	+		+		R	11	0
				AT	2	0		0	+	R	23	0
14				S	2,250	+		+	0	R	17	0
				AT	800	0		+ Vent.	0	D	2 hr.	+
10			11.0	0	12,000	+		+	0	R	14	0
				0	12,000	+		+		D	12 hr.	0
8				AT	1,596	+		+	0	R	11	0
				S	18	0		0	+	D	17 hr.	0
24				AT	1,500	0		+	+	R	27	0
5		S.F. 4.1		AT+S	13,900	+		+	0	R	12	0
12	S.F. 14.9	S.F. 9.1		0	810	+		+	+	R	12	0
8			S.F. 12.3	0	7,680	+		+	0	D	8	0
19				AT+S	15,960	+		+	+	R	19	0
				0	?	0		0	+	D	5 hr.	0
3				0	6	0		0	0	D	14	0
				L.P. 6 days later showed 51,600 cells; gram-negative diplococci were seen, and meningococci were cultured from this fluid								
18		8.2		0	6,000	0		+	0	R	20	0
				0	Bloody 200	0		0	+	D	4 hr.	0
20	9.7	15.7		0	12,800	+		+	0	R	25	0
7	4.0	4.6		0	10,000	+		0	+	R	13	0
8	SP	SA	SP	AT	1,060	+		+	0	R	22	0
	33.2	23.1	14.7									
	SA	SP	SA									
	22.8	33.4	10.2									
22		19.3	21.3	S	4,100	+		+		R	30	0
15	24.6	35.7	18.9	0	720	+	+	+	0	R	20	0
12	34.5	37		0	14,800	+		+	0	R	19	0
3				0					+	R	3 days	0
14	14.5	42	47	0	15,250	+		+	0	R	16	0
2	38			S	34,000	+	+	+	0	D	2	0
9	26.9	52.5	44.7	0	3,600	+	+	+	0	R	15	0
14	22.2	48.0		0	4,900	+	+	+	+	D	22	0
10	29.7	20.2	12.7	0	3,800	+	+	0	0	R	18	0
				0	4	0		0	P.M. +	D	1 hr.	0
10	24.2	25.2		0	12,600	+		+	0	R	12	0
14	SD	SD		0	24,250	+	14 hr. +	+	0	R	22	0
	21.6	22.6										
		SA										
		17.9										
13	22.8	45.3	21.7	0	10,640	+	+	0	0	R	15	0
5	26.4	24	16.3	0	4,300	?		+	0	R	8	0
13				0	5,630	+	+	+	+	R	15	0
9	30.0	43.7		0	1,600	0	0	0	0	R	15	12 Gm. ST
				Sp. Fl. culture positive in hosp. at Alton, Illinois								
15	31.4		44.4	0	10,750	0		+	0	R	18	0
7	36.2	45.6	53.0	0	7,500	+		+	0	R	14	0
11	SD	SA	SA	0	2,000	+	+		+	R	14	0
	44.4	23.6	17.9									
9	22.3	13.5	20.0	0	13,550	+		+	0	R	12	0
5	19.4	14.9	10.2	0	9,000	0	+	0	0	R	12	0
10	30.4			0	21,500	+		+	0	R	12	0
12	30.7	48.8	40.4	0	32,000	+		+	+	R	13	0
9	23.9		4.7	0	9,800	?		+	+	R	14	0
11	30.7	S.F. 45.0		0	270	+		+	0	R	11	0
7	52.4	48.8		0	7	0		0	+	R	13	0
8	34.7	18.7	10.2	0	6	0	0	0	on egg +	R	10	.5 Gm. ST
6	28.3	21.1	14.7	0	19,800	+	+	+	0	R	25	0
10	22.4	20.5	18.8	0	5,775	+	+	0	0	R	12	0
8	28.8	16.3	19.5	0	7,250	+	+	+		R	14	0
16			6.5	0	8,900	0	+	+	0	R	23	0
13	11.4	18.4	8.7	0	7,200	+		0	0	R	24	0
12	24.0	17.8	9.7	0	9,000	+		+	0	R	15	0

TABLE

CASE	DATE OF ADMISSION	HISTORY NO.	SEX	AGE	BODY WT. (KG.)	APPARENT DAY OF MENINGITIS WHEN THERAPY WAS BEGUN	SULFONAMIDE				
							DRUG USED	TOTAL GM.	ROUTE ADMINISTERED		
									IV	SC	IT	ORAL
54	1/ 7/44	U-128	M	2½ yr.	10.0	1 day	SM	13.0	0	0	4.0	9.0
55	1/16/44	U-162	F	4 yr.	15.0	3 wk.	SD	35.5	0	0	9.5	26.0
56	1/17/44	U-172	M	8 yr.	24.0	10 hr.	SM	30.8	0	0	0	30.8
57	1/19/44	U-181	F	11 mo.	9.0	3 days	SD	29.4	0	6.4	0	23.0
58	1/21/44	U-199	F	5 yr.	16.8	1 day	SM	40.8	0	0	7.0	33.8
59	1/26/44	U-224	M	8 yr.	25.4	1 day	SD	75.5	0	0	67.5	8.0
60	1/28/44	U-236	F	14 mo.	8.6	1 day	SD	36.0	0	0	3.0	33.0
61	2/ 1/44	U-261	F	1½ yr.	11.1	1 day	SD	21.7	0	10.7	0	11.0
62	2/12/44	U-318	F	4 yr.	12.0	2½ days	SM	29.0	0	9.0	0	20.0
63	2/14/44	U-332	M	9 mo.	9.1	3 days	SM	17.5	0	5.0	0	12.5
64	2/19/44	U-366	F	2 yr.	10.0	3 days	SD	20.5	0	6.5	0	14.0
65	2/22/44	U-388	M	3 yr.	16.8	1½ days	SM	31.0	0	13.6	0	17.4
66	2/25/44	U-411	M	9 mo.	9.2	4 days	SD	18.3	0	7.3	0	11.0
67	2/28/44	U-432	M	4½ yr.	15.4	3 days	SM	58.5	0	6.0	0	52.5
68	3/ 3/44	U-455	F	3 yr.	13.6	3 days	SM	24.8	0	7.8	0	17.0
69	3/ 6/44	U-469	F	6 mo.	8.2	1 day	SM	14.8	0	7.5	0	7.25
70	3/10/44	U-500	F	4 yr.	14.0	11 hr.	SD	23.4	0	1.4	0	22.0
71	3/ 2/44		F	3 yr.	13.4	1 day	SD	21.0	0	9.0	0	12.0
72	3/16/44	U-548	M	9 yr.	34.0	1 day	SM	95.4	0	22.0	0	73.4
73	3/20/44	U-580	M	5 yr.	15.5	4 days	SD	42.3	0	16.0	0	26.25
74	3/25/44	U-611	M	2 yr.	11.0	1 day	SD	24.8	0	9.9	0	14.9
75	3/31/44	U-645	M	22 mo.	11.8	1 day	SD	5.0	0	5.0	0	0
							SA	31.5		31.5		
76	4/13/44		M	13 yr.	?	2 days	SM	5.0	0	5.0	0	0
77	4/16/44		M	22 mo.	11.3	1 day	SD	15.4	0	7.4	0	8.0

that 3 patients showed bilateral adrenal hemorrhage (Waterhouse-Friderichsen syndrome). One patient had meningococcal pericarditis. The other findings at autopsy for this group were not especially noteworthy.

SUMMARY AND CONCLUSIONS

We have analyzed 77 patients with meningococcal infections seen at the St. Louis Children's Hospital between the years 1937-1944. The years 1937-1942 represent nonepidemic years, and 1943-1944 represent epidemic years.

As we gained more and more experience with the use of sulfonamide drugs in meningitis, we have come to certain fundamental conclusions.

We believe that intensive parenteral chemotherapy by the subcutaneous route is the treatment of choice of purulent meningitis for the first twenty-four to forty-eight hours or until the etiological organism is proved to be a meningococcus and that blood levels for the first few days of treatment should range between 20 and 40 mg. per cent. This level of drug, we feel, is adequate to cope even with the most serious meningidities; that is, pneumococcal or influenzal. Although such intensive chemotherapy probably enhances somewhat the possibility for kidney complications, when such precautions as adequate hydration, alkalization of the urine, careful records of daily intake and output, and daily urine examinations are taken, serious difficulties are rare. As soon as the etiological organism is definitely established as the meningococcus

TABLE I—CONT'D

THERAPY					BACTERIOLOGICAL DATA							
TOTAL NO. OF DAYS ON DRUG	CONCENTRATION MG./100 C.C. 2ND DAY	3RD DAY	4TH DAY	SERUM THERAPY	SP. FLUID SMEAR CELLS	SP. FLUID SMEAR ORG.	CULTURE EGG	CULTURE BL. AGAR	BLOOD CULTURE	OUTCOME	DAYS IN HOSP.	THERAPY BEFORE ENTRY
12	21.9			0	1,800	+		+		R	12	0
13		7.2	11.4	0	4,200	0	+	0	0	R	17	0
11		26.2		0	4	0	0	0	+	R	12	0
6	44.5	10.7	5.8	0	7,050	+	+	0		R	12	0
9	12.1			0	8,800	+		+		R	14	1 Gm. sulfonamide
13	27.7	17.4		0	315	+		+	0	R	18	0
11			S.F. 2.2	0	4,200	+		+	0	R	17	0
7	24.6	12.5		0	5,600	0	+	+	0	R	10	0
10	26.5	16.2	16.2	0	25,000	+		+	0	R	12	0
14	20.6		13.9	0	1,100	+		0	0	R	18	0
10		8.2		0	5,500	+	8th day +	0		R	11	0
13	25.9	40.4	22.9	0	4,200	+		+	0	R	17	0
8			4.8	0	12,000	+	+	+		R	10	0
15	28.6		10.5	0	6,000	+		+	0	R	17	0
8	26.5			0	opalescent	0	+			R	10	0
7	33.2	27.2	11.1	0	3	0	0	0	+	R	9	0
7				0	7,400	+	+		0	R	8	0
6	24.8	16.8		0	10	0		+	0	R	14	.5 Gm. sulfonamide
14	34.0	33.0	23.9	0	3,200	+	+	0	0	R	24	0
13	13.2	22.6	8.0	0	3,770	+	+		0	R	16	0
7	28.3	17.3	9.9	0	opaque	+		+	0	R	16	0
12	25.4			0	4,000	+		+	0	R	18	2.5 Gm. SD
9 hr.				0	4,104	+		+		D	9 hr.	0
6	28.2			0	11,350	?	0	+	0	R	7	0

and the clinical course has exhibited a favorable trend, then the patient may be safely maintained on 0.3 Gm. per kilogram of body weight of a sulfonamide.

We do not believe that serum therapy sufficiently enhances the effectiveness of sulfonamide therapy to justify its use routinely.

Adequate hydration is of utmost importance, and we strive for a minimum of 10 per cent of the body weight in fluids per day.

Alkalinization of the urine is important, and we believe that the easiest and most effective means is by the administration of sodium lactate either parenterally or enterally.

Accurate daily records of the patient's intake and output are important as well as daily examinations of the urine and regular white blood cell counts, especially during the second week of chemotherapy.

There were comparatively few complications. The one most frequently encountered was a generalized arthritis which cleared spontaneously. The most serious complication which remained as a permanent residual was bilateral nerve deafness. We encountered 2 cases of postinfectious encephalitis.

The uncorrected mortality rate was 14.2 per cent. If the one patient who died of another disease and the 7 patients who expired after being in the hospital less than twenty-four hours are excluded (3 receiving no treatment), the mortality rate for the seven-year-period is 3.8 per cent.

TABLE II

NO.	HISTORY NO.	AGE	SEX	DURATION OF ILLNESS	THERAPY BEFORE ENTRY	THERAPY AT HOSPITAL	HOSPITAL STAY	AUTOPSY FINDINGS
1	S-2951	11 mo.	F	3 wk.	0	Serum + 4.8 Gm. SD	2 da.	Bronchopneumonia of all lobes of the lungs Meningitis
2	S-3067	2 yr.	M	1 da.	0	40 Gm. SD	22 da.	No autopsy Developed bronchiolitis on 15th hosp. day, tracheotomy performed
3	N-748	6 mo.	M	26 da.	70,000 units Antitoxin	0	2 hr.	Purulent meningitis—organizing exudate over surface of brain Internal hydrocephalus
4	N-914	6 yr.	M	1 da.	0	50,000 units Antiserum + 5 Gm. SA	17 hr.	No autopsy
5	N-1943	5 mo.	M	2 da.	0	0	12 hr.,	Hemorrhages and focal necrosis of spleen Purulent meningitis
6	O-869	6 mo.	M	2 wk.	0	11 Gm. SA	8 da.	No autopsy
7	P-210	6 mo.	F	4 da.	0	5.5 Gm. SP	14 da.	No autopsy
8		13 yr.	M	2 da.	0	5 Gm. SM	9 hr.	Pericarditis—purulent meningitis Bilateral adrenal hemorrhage
9	O-2269	2½ yr.	M	1 da.	0	2 Gm. SA	5 hr.	Nothing of note
10	Q-2485	4 yr.	M	1 da.	0	1½ Gm. SP	4 hr.	Bilateral adrenal hemorrhage
11	T-261	4 mo.	M	1 da.	0	0	1 hr.	Bilateral adrenal hemorrhage

B. EXPERIENCES AT THE ST. LOUIS ISOLATION HOSPITAL

This is a report on 209 cases (Table III) of meningococcal infection at the Isolation Hospital of St. Louis, Mo., admitted between January of 1942 and August of 1943. The patients were drawn from an area which includes the City and County of St. Louis and neighboring communities in the states of Missouri and Illinois. Since the Isolation Hospital is the center for the treatment of contagious diseases in this area, this number represents the majority of hospital treated cases.

For several years prior to 1942, cases of meningococcal infection seen at Isolation Hospital were few and averaged 12 per year for the five-year period dating back to 1937. In 1942, 26 cases were reported to the St. Louis Health Department, and 13 patients were treated in this hospital and were included in this report. In 1943, 342 local cases were reported, 245 occurring in the seven-month period from January to August. In this same seven-month period, 196 patients (resident and nonresident) were admitted to the Isolation Hospital and are included in this report. The 1943 epidemic of meningococcic meningitis is thought to be the most extensive epidemic of disease recorded in this country; it was estimated[1] that approximately 17,000 cases were recognized.

Upon examining the distribution of cases in metropolitan St. Louis (see map, Chart V) it is apparent that the majority of patients came from the east-central section of the city bordering on the Mississippi River. In this section living conditions are very poor, and the houses are old and overcrowded. In view of this fact it is interesting that we found but few instances where more than one person in the family developed the disease. The following are the only instances recorded of more than one infection within a family:

(1) G. S. (1183-42) developed meningococcic meningitis nine days after her mother developed the disease. (The patient's mother was treated in another St. Louis hospital.)

(2) M. R. (1326-42) had meningococcic meningitis, and her sister, L. R. (1351-42), entered the hospital a few days later with meningococcemia.

(3) W. L. (223-43) was found to have a meningococcemia upon admission. The sister of this patient, J. L. (224-43), was admitted the following day with meningococcus meningitis and meningococcemia.

(4) The following group of children, B. D. (180-43), B. W. (193-43), and B. G. (171-43), represents three families. They all slept in one room and were admitted during the period of one week. B. G. was found to have meningococcus meningitis, and B. D. and B. W. were found to have fever, petechial rashes, and elevated cell counts in the spinal fluid without meningeal symptoms.

TABLE III

PATIENT	HOSP. NO.	RACE, SEX, AGE	HOURS OF ILLNESS BEFORE ENTRY	DIAGNOSIS					THERAPY BEFORE ENTRY	DRUG USED & TOTAL DOSE IN GM.	MAXIMUM DRUG LEVEL MG./100 C.C.	SERUM USED	TOTAL DAYS ON DRUG	TOTAL DAYS IN HOSP.	COMPLICATION		RESULT OF THERAPY
				TYPICAL SKIN RASH	SPINAL FLUID			ORG. FROM BLOOD CULTURE							FROM DRUG	FROM DISEASE	
					CELLS	ORG. ON SMEAR	ORG. ON CULTURE										
1	105-42	WM24	24	0	4,200	+	+	+	0	SD 140.0	11	0	13	16	0	0	Recovered
2	653-42	WM6	24	+	800	+	+	+	0	SD 56.5	14	0	9	11	0	0	Recovered
3	1090-42	WF29	18	+	120	0	+	+	0	SD 51.0	7	0	12	17	0	0	Recovered
4	1144-42	WM45	36	+	13,500	+	0	0	0	SD 15.5	10	0	1.5	1.5	+	0	Died
5	1148-42	WM28	108	+	680	0	0	0	SA 12	SD 81	20	0	8	11	0	0	Recovered
6	1149-42	WM37	48	+	11,000	+	0	0	?	SD 111	27	0	18	18	0	+	Recovered
7	1175-42	WM17	24	+	1,500	+	0	0	SD 5	SD 76	12	0	11	12	0	0	Recovered
8	1367-42	WM51	?	+	8,750	0	0	0	SD ?	SD 112	19	0	13	13	0	0	Recovered
9	1379-42	WF2	72	0	4,000	+	0	+	SD ?	SD 30.5	41	0	8	13	0	0	Recovered
10	1384-42	WF14	48	+	6,800	0	+	0	0	SD 105	58	0	19	21	0	0	Recovered
11	1513-42	WF48	96	+	26,000	+	+	0	SD 41	SD 76	7	0	9	11	0	0	Recovered
12	1538-42	WM28	48	+	9,200	+	0	0	SD 5	SD 71	13	0	7	9	0	0	Recovered
13	1539-42	WM7	24	+	3,600	0	+	0	0	SD 102	30	0	13	17	0	0	Recovered
14	1542-42	WM6	24	0	6,250	+	+	+	0	SD 110.5	19	0	12	29	0	+	Recovered
15	1544-42	CF28	24	+	25,000	+	+	+	0	SD 88	22	0	10	15	0	0	Recovered
16	1557-42	WF18	24	+	18,250	+	+	0	0	SD 96	13	0	10	11	0	0	Recovered
17	1559-42	WF3mo.	96	0	4,050	+	+	0	0	SD 66.5	34	0	30	38	0	0	Recovered
18	1568-42	WM4	?	+	15,500	0	0	0	ST 1.5	SD 43	16	0	9	14	0	0	Recovered
19	1575-42	CM8	120	0	8,000	+	+	0	0	SD 60	29	0	11	14	0	0	Recovered
20	1576-42	WM33	72	+	8,000	+	+	0	ST 1.0 Neopr. 5c.c.	SD 52	12	0	9	11	0	0	Recovered
21	1586-42	WF56	72	+	10,575	0	0	0	0	SD 61	23	0	8	13	0	0	Recovered
22	1608-42	WM17	72	+	2	0	+	+	?	SD 51	14	0	5	6	0	0	Recovered
23	1611-42	WF1	72	0	360	+	+	0	ST ?	SD 35	21	0	8	12	0	0	Recovered
24	1631-42	WM2	24	+	10,125	+	+	+	0	SD 28	30	0	11	14	0	0	Recovered
25	1639-42	WF48	60	?	2,250	+	0	0	ST 9	SD 56	21	0	7	11	0	0	Recovered
26	1643-42	WF32	72	+	4,750	0	0	0	SD 35	SD 93	66	0	6	17	+	+	Recovered
27	1644-42	WM30	72	+	2,100	0	0	0	S 6	SD 60	16	0	6	9	0	0	Recovered
28	1650-42	WM34	48	+	3,400	+	+	+	ST 2	SD 22	21	0	3	13	0	0	Recovered
29	1651-42	CF9	48	0	12,960	+	+	0	0	SD 72	21	0	11	12	0	0	Recovered
30	1654-42	WM13	36	+	12,200	+	+	+	0	SD 87	12	0	9	12	0	0	Recovered
31	1657-42	WM8	24	+	5,760	+	0	0	0	SD 34	28	0	8	12	0	0	Recovered
32	1703-42	WF49	72	+	14,000	0	0	0	SA 8	SD 110	—	0	13	16	0	0	Recovered
33	1763-42	WF56	?	+	7,750	+	+	+	0	SD 90	41	50,000 U	9	13	0	0	Recovered
34	1785-42	WF3	120	+	3,300	+	0	0	0	SD 96	41	0	12	14	0	0	Recovered
35	1801-42	WM2.5	48	+	7,600	+	0	0	SD 1.5	SD 64.5	41	0	7	12	0	0	Recovered
36	1823-42	WF26	120	+	7,400	0	+	0	0	SD 48	21	0	5	9	0	0	Recovered
37	1829-42	WF8	24	+	26	0	+	0	ST 2.5 SP 7	SD 50	34	0	8	12	0	0	Recovered

38	1830-42	WF57	24	+	13,350	+	+	0	0	SD 117	27	0	11	14	0	0	Recovered
39	28-43	WF46	120	+	8,950	+	+	0	0	SD 83	29	0	8	11	0	0	Recovered
40	30-43	WF26	48	+	8,300	0	0	0	SD 12	SD 49.5	41	0	8	12	0	0	Recovered
41	40-43	WM52	240 ?	0	2,000	0	+	0	0	SD 74	19	0	10	23	0	+	Recovered
42	48-43	WF22	48	0	11,500	0	+	0	S 4	SD 132	32	0	11	14	0	0	Recovered
43	53-43	WF23	72	+	4,200	+	0	0	SD ?	SD 56	11	0	9	13	0	0	Recovered
44	84-43	WM43	48	+	cloudy	+	+	+	0	SD 76	22	0	10	13	+	+	Recovered
45	91-43	WM4mo.	30	+	700	+	0	0	0	SD 2	—	30,000 U	0.5	0.5	0	0	Died
46	106-43	WM61	?	0	3,400	+	0	0	SD 5	SD 73	29	0	12	13	0	+	Recovered
47	132-43	WM29	48	+	6,450	+	+	0	S ?	SD 53	16	0	7	9	0	0	Recovered
48	160-43	WF41	168 ?	+	20,000	0	0	0	0	SD 32.5	19	0	4	11	+	0	Recovered
49	169-43	CF55	72	+	10,575	+	+	0	SD ?	SD 47	21	0	9	13	0	0	Recovered
50	176-43	CM65	18	0	cloudy	0	+	0	0	SD 25	34	0	3-	60 hr.	0	0	Died
51	189-43	WM4	24	+	22,500	0	0	0	0	SD 24	34	0	7	10	0	0	Recovered
52	190-43	WM45	108	+	2,700	+	+	0	0	SD 80	15	0	8	11	0	0	Recovered
53	221-43	CF2	48	+	5,240	+	+	+	0	SD 22	41	40,000 U	12	114	0	0	Recovered
54	222-43	WF16	72	+	4,250	0	0	0	0	SD 107	23	50,000 U	10	13	0	0	Recovered
55	193-43	WF2	36	+	80	0	0	0	0	SD 19	13	0	17	19	0	0	Recovered
56	230-43	CF67	12	0	7	0	+	+	0	SD 25	41	0	4	4	0	0	Died
57	240-43	WM37	120	+	1,045	0	0	0	0	SD 64	14	0	10	13	0	0	Recovered
58	260-43	WM21	36	+	15,015	?	+	+	0	SD 84	6	50,000 U	11	15	0	+	Recovered
59	285-43	WM15	48	+	21,000	+	+	0	0	SD 50	26	0	7	9	0	0	Recovered
60	289-43	WM17	24	+	13,600	+	0	0	0	SD 67	15	0	9	11	0	0	Recovered
61	305-43	CM11	36	0	3,100	+	+	0	0	SD 32	12	40,000 U	5	10	0	0	Recovered
62	306-43	CM34	240 ?	0	5,440	+	0	0	ST 5	SD 56	13	0	6	8	0	0	Recovered
63	309-43	CF3	72	+	4,500	0	0	+	0	SD 2	—	20,000 U	0	3 hr.	0	0	Died
64	325-43	WM4	72	0	22,100	+	+	0	0	SD 19	17	0	5	9	0	0	Recovered
65	335-43	CM12	48	+	30,000	+	+	0	0	SD 91	12	60,000 U	12	17	0	+	Recovered
66	360-43	WF7	24	+	21,960	?	0	0	0	SD 32.5	—	0	7	15	0	0	Recovered
67	366-43	WM56	168	+	9,856	+	0	0	0	SD 75	—	50,000 U	7	18	0	+	Recovered
68	369-43	WF62	36	+	25,000	+	+	+	0	SD 5	—	40,000 U	1-	19 hr.	0	0	Died
69	385-43	WM5	30	+	7,250	0	0	0	0	SD 18.5	29	40,000 U	3	11	+	0	Recovered
70	386-43	CM4	12	+	117	0	0	+	0	SD 20	24	40,000 U	5	14	0	0	Recovered
71	389-43	WM45	24	+	35,700	+	+	0	0	SD 88	7	0	9	12	0	0	Recovered
72	425-43	CM2.5	48	+	10,125	0	0	0	ST ?	SD 22.5	22	0	7	11	0	0	Recovered
73	435-43	WF26	168	0	16,600	+	0	0	0	SD 113.5	8	0	11	13	0	0	Recovered
74	468-43	CM1	48	0	3,500	+	+	+	0	SD 19.3	39	30,000 U	9	11	0	0	Recovered
75	483-43	WF58	168 ?	+	15,500	+	0	0	0	SD 70	10	0	10	12	0	0	Recovered
76	497-43	WM5	48	+	46,000	0	+	0	0	SD 35	23	40,000 U	11	14	0	0	Recovered
77	509-43	WF35	24	+	5,666	+	+	0	0	SD 41	10	0	7	9	0	0	Recovered
78	567-43	WM31	48	+	6,400	+	+	0	0	SD 94	13	0	9	11	0	0	Recovered
79	568-43	WF3	72	+	1,500	+	+	+	0	SD 32.5	—	0	11	18	0	+	Recovered
80	570-43	WM52	96	0	8,100	+	0	0	SD 5	SD 66	16	0	7	9	0	0	Recovered
81	573-43	WF1	72	+	3,450	+	+	+	0	SD 9.8	22	20,000 U	5	9	0	0	Recovered
82	603-43	WF19	48	0	10,000	+	0	0	SD ?	SD 53	11	0	6	8	0	0	Recovered
83	617-43	CM19	24	+	500	0	0	0	0	SD 39	9	0	5	7	0	0	Recovered
84	649-43	WM20	120	0	13,750	0	+	+	0	SD 52	—	0	9	13	0	0	Recovered
85	673-43	WM49	96	0	3,200	+	0	0	ST 5	SD 55	7	0	7	8	0	0	Recovered

S = Unknown sulfonamide; SA = Sulfanilamide; SD = Sulfadiazine; SP = Sulfapyridine; ST = Sulfathiazole; SM = Sulfamerazine; SPZ = Sulfapyrazine.

TABLE III—CONT'D

PATIENT	HOSP. NO.	RACE, SEX, AGE	HOURS OF ILLNESS BEFORE ENTRY	DIAGNOSIS					THERAPY BEFORE ENTRY	DRUG USED & TOTAL DOSE IN GM.	MAXIMUM DRUG LEVEL MG./100 C.C.	SERUM USED	TOTAL DAYS ON DRUG	TOTAL DAYS IN HOSP.	COMPLICATION		RESULT OF THERAPY
				TYPICAL SKIN RASH	SPINAL FLUID			ORG. FROM BLOOD CULTURE							FROM DRUG	FROM DISEASE	
					CELLS	ORG. ON SMEAR	ORG. ON CULTURE										
86	682-43	WF3	36	0	14,000	+	0	0	0	SD 32	28	0	12	18	0	+	Recovered
87	705-43	WM39	96	0	9,000	0	+	0	ST 5	SD 66	8	0	13	16	0	0	Recovered
88	748-43	WF7	120 ?	+	3,000	+	+	0	0	SD 36	12	0	6	8	0	0	Recovered
89	755-43	WM16	48 ?	+	2,400	0	0	0	0	SD 45	11	0	8	9	0	0	Recovered
90	762-43	WM8	24	+	5,250	+	+	+	0	SD 30	41	0	8	9	0	0	Recovered
91	796-43	WF10	48	+	14,000	0	0	0	0	SD 30	23	0	6	8	0	0	Recovered
92	842-43	WM12	36	+	12,500	0	+	0	0	SD 39	13	0	11	12	0	0	Recovered
93	886-43	CM4	72	+	3	0	0	+	0	SD 8	—	0	5	7	0	0	Recovered
94	899-43	WF57	36	+	20,300	+	0	+	0	SD 64	24	0	12	15	0	0	Recovered
95	958-43	WM45	36	+	10,000	+	+	0	0	SD 54	—	0	9	11	0	+	Recovered
96	1014-43	CF14	24	+	25,000	+	+	0	0	SD 16	26	0	3	3	0	0	Recovered
97	1023-43	CF19mo.	24	+	2,500	0	+	0	0	SD 15	—	0	8	13	0	0	Died
98	1146-42	WF30	36	+	21,700	+	+	0	SP 7.5	SD 99	7	0	11	13	0	0	Recovered
99	1572-42	CM24	24	+	22,750	0	+	+	SA 2	SD 134.5	22	0	27	33	+	+	Recovered
100	614-42	WF52	120	+	1,100	+	0	0	0	ST 74							
101	1150-42	WM39	48	+	5,000	?	0	0	0	SD 38	9	0	7	12	0	0	Recovered
102	1177-42	CM4	48	+	3,700	+	0	+	SD 0.5	SA 4							
103	1183-42	WF31	24	+	1,242	+	0	0	0	SD 32	30	0	4	17	0	0	Recovered
104	1469-42	WM17	24	+	6,000	+	+	+	0	SA 2							
105	1590-42	WM4	48	+	1,260	+	+	+	0	SD 56	32	0	16	19	0	+	Recovered
106	1746-42	CM52	48	+	21,600	+	0	0	0	SA 17							
107	21-43	WM30	24	+	20,600	+	+	+	0	SD 21.5	32	0	4	15	0	0	Recovered
108	129-43	CF6	96	0	28.250	+	+	0	0	SA 1.0							
109	195-43	WM29	72	0	18,600	0	+	0	0	SD 14	21	0	10	15	+	0	Recovered
110	234-43	WM5	48	0	15	0	0	+	0	SA 141							
111	235-43	WM7	24	+	13	0	0	+	0	SD 14	53	0	7	10	+	0	Recovered
										SA 26							
										SD 58	17	0	12	15	0	0	Recovered
										SA 79							
										SD 68	19	0	11	13	0	0	Recovered
										SA 46							
										SD 27.5	58	0	9	11	0	0	Recovered
										SPZ 24							
										SD 58	15	40,000 U	11	14	0	0	Recovered
										SA 39							
										SD 7	31	0	7	10	+	+	Recovered
										SA 15							
										SD 13.2	48	40,000 U	5	13	+	0	Recovered
										SA 8							

112	245-43	WM23	48	+	8,640	?	0	0	0	SD 15 SA 23	15	0	6	10	+	0	Recovered
113	320-43	CM6	24	+	10,000	0	0	+	0	SD 12.5 SA 27	41	0	9	14	+	0	Recovered
114	337-43	CM42	24	0	3,900	+	+	+	0	SD 95 SA 17	15	50,000 U	10	19	0	0	Recovered
115	356-43	WM31	48	+	15,500	0	0	+	SD 5	SD 15 SA 46	7	0	6	9	+	0	Recovered
116	432-43	CF2	24	+	10,500	0	+	0	0	SD 7.2 SA 9.8	41	0	5	10	+	0	Recovered
117	506-43	CF25	24	+	1,760	+	+	+	0	SD 20 SA 35	18	50,000 U	9	12	0	0	Recovered
118	534-43	WM8	24	+	3,500	+	+	0	0	SD 13 SA 39	23	0	6	10	+	0	Recovered
119	1153-42	WM6	72	+	7,100	+	+	+	0	SM 38	20	0	13	14	0	0	Recovered
120	1266-42	WF14	48	+	12,000	+	+	+	Neopr. 1.4	SM 62	22	0	9	13	0	0	Recovered
121	1318-42	WF24	72	+	3,950	+	0	0	0	SM 42	26	0	8	10	0	0	Recovered
122	1351-42	WF7	20	+	24	0	0	+	0	SM 21	18	0	7	10	0	0	Recovered
123	1365-42	WF17	36	+	19,000	+	+	0	0	SM 38	19	0	12	14	0	0	Recovered
124	1366-42	WM24	72	0	25,000	+	+	0	0	SM 34	13	0	10	11	0	0	Recovered
125	1378-42	WM2	48	0	22,000	+	+	+	0	SM 45.5	30	0	10	14	0	0	Recovered
126	1412-42	WM16	72	+	38,000	0	+	0	0	SM 61.5	11	0	12	14	0	0	Recovered
127	1446-42	WF12	36	+	12,500	0	+	0	0	SM 20	19	0	4	9	+	0	Recovered
128	1622-42	WM15	24	0	5,330	+	0	0	0	SM 32	15	0	6	9	0	0	Recovered
129	1424-42	WM38	?	0	3,105	+	+	0	0	SM 52	21	0	9	13	0	0	Recovered
130	1445-42	WF20	96	+	160	+	+	+	0	SM 60	25	0	9	12	0	0	Recovered
131	1483-42	CM18	24	+	3,300	+	0	+	0	SM 90	27	0	14	18	0	0	Recovered
132	1508-42	WF20	24	0	12,000	+	+	+	0	SM 50	21	0	9	11	0	0	Recovered
133	1525-42	WM14	48	+	3,760	+	+	+	0	SM 44	20	0	10	18	+	0	Recovered
134	1533-42	WF17	24	0	17,500	0	+	0	0	SM 35	17	0	5	9	0	0	Recovered
135	1534-42	WF25	96	+	13,000	+	+	0	0	SM 41	12	0	7	12	0	+	Died
136	1531-42	WF65	?	0	19,200	+	0	0	0	SM 22	15	0	4	4	0	0	
137	1593-42	CF19	36	0	1,300	+	+	+	0	SM 36	22	0	6	9	+	0	Recovered
138	1602-42	WF67	48	0	56,000	0	+	+	0	SM 21	6	0	2	2	0	0	Died
139	1627-42	WM24	72	+	19,600	+	+	0	0	SM 142	9	0	17	26	0	+	Recovered
140	1647-42	WM60	?	+	96	0	+	0	0	SM 12	16	0	1	1	0	0	Died
141	1666-42	WM14	24	+	18,450	+	+	0	0	SM 43.5	13	0	8	9	0	0	Recovered
142	1698-42	WM34	48	+	35,200	+	+	0	0	SM 52	16	0	8	10	0	0	Recovered
143	1721-42	WF35	36	0	1,600	0	+	0	0	SM 41	17	0	7	8	0	0	Recovered
144	1730-42	WF32	48	+	17,250	+	+	0	0	SM 46	30	0	8	15	0	+	Recovered
145	1805-42	WF15	24	0	11,200	+	0	0	0	SM 54	14	0	10	13	0	0	Recovered
146	1810-42	WF21	24	+	27,500	+	+	0	0	SM 38	15	0	5	10	+	0	Recovered
147	13-43	WM14	20	+	11,800	0	0	0	0	SM 38	14	0	7	11	0	0	Recovered
148	33-43	WM15	24	+	8,100	0	+	+	0	SM 64	23	0	10	16	0	+	Recovered
149	35-43	WF23	96	0	30,000	+	+	0	0	SM 56	20	0	10	12	0	0	Recovered
150	109-43	CF6	60	+	18,000	0	0	0	0	SM 27	35	50,000 U	13	15	0	0	Recovered

TABLE III—CONT'D

PATIENT	HOSP. NO.	RACE, SEX, AGE	HOURS OF ILLNESS BEFORE ENTRY	DIAGNOSIS					THERAPY BEFORE ENTRY	DRUG USED & TOTAL DOSE IN GM.	MAXIMUM DRUG LEVEL MG./100 C.C.	SERUM USED	TOTAL DAYS ON DRUG	TOTAL DAYS IN HOSP.	COMPLICATION		RESULT OF THERAPY
				TYPICAL SKIN RASH	SPINAL FLUID			ORG. FROM BLOOD CULTURE							FROM DRUG	FROM DISEASE	
					CELLS	ORG. ON SMEAR	ORG. ON CULTURE										
151	145-43	CM9	60	+	4,800	?	+	+	0	SM 8 SA 48	16	40,000 U	11	21	0	+	Recovered
152	1326-42	WF10	24	+	19,000	+	0	0	0	SM 8 SP 57	—	0	10	14	0	0	Recovered
153	1496-42	WM52	?	+	9,500	+	+	0	0	SM 117 SP 35	24	0	20	20	+	0	Died
154	1626-42	WF21	24	+	180	+	+	+	0	SM 22 SA 13 SD 102	—	0	17	47	+	0	Recovered
155	755-42	WF14	24	+	10,250	?	+	0	0	SPZ 94	22	0	11	15	0	0	Recovered
156	1674-42	WF8	72	0	6,200	0	+	0	0	SPZ 42	36	0	9	13	0	0	Recovered
157	1695-42	WF10wk.	24	+	279	0	+	+	0	SPZ 1[illegible]	29	0	9	14	0	0	Recovered
158	1779-42	WF3	24	+	276	+	+	0	0	SPZ 97.5	29	40,000 U	18	22	0	+	Recovered
159	1782-42	WM7	24	+	30,240	+	+	0	0	SPZ 132	31	0	13	17	0	0	Recovered
160	1706-42	WM4	48	+	2,280	0	+	0	0	SPZ 74	13	0	13	16	0	0	Recovered
161	1786-42	WF11	24	+	?	+	+	0	0	SPZ 96	40	50,000 U	10	16	0	0	Recovered
162	1-43	WM9	24	+	11,300	+	+	0	0	SPZ 49	48	30,000 U	7	12	0	0	Recovered
163	13-43	CF10	24	+	7,240	+	+	0	0	SPZ 80.7	36	0	10	18	0	0	Recovered
164	31-43	WM2	60	0	20,250	+	+	0	0	SPZ 38	45	0	13	17	0	0	Recovered
165	39-43	WM15mo.	24	+	12,620	0	0	0	0	SPZ 46	16	0	10	14	0	0	Recovered
166	165-43	WM2	96	+	6,750	+	0	0	0	SPZ 34	30	30,000 U	9	14	+	0	Recovered
167	171-43	WM3	24	+	24,975	+	+	0	0	SPZ 25	32	0	6	14	0	0	Recovered
168	179-43	CF5	?	0	10,000	+	0	0	0	SPZ 20	33	40,000 U	13	16	0	0	Recovered
169	180-43	WF4	24	+	9	0	0	0	0	SPZ 32	36	0	7	23	+	0	Recovered
170	223-43	WF2.5	12	+	6	0	0	+	0	SPZ 19	34	30,000 U	12	13	0	0	Recovered
171	224-43	WF4	24	+	26,000	+	+	+	0	SPZ 18	36	40,000 U	7	10	0	0	Recovered
172	259-43	WF4	96	0	2,000	+	+	0	0	SPZ 32.5	26	0	7	13	0	0	Recovered
173	297-43	CF9	72	0	2,250	+	+	+	0	SPZ 38	25	40,000 U	10	10	0	0	Recovered
174	307-43	WF2	24	+	2,950	0	+	+	0	SPZ 19.3	17	30,000 U	9	11	0	0	Recovered
175	1761-42	WF13	48	+	7,500	?	+	0	0	SPZ 57 SD 21	20	0	8	12	0	0	Recovered
176	300-43	WF6	72	+	4,250	0	+	0	0	SPZ 18.3 SA 17.5	45	0	8	10	+	0	Recovered
177	130-43	WM2	24	+	440	0	0	+	0	SPZ 10 SA 8	39	40,000 U	8	12	+	0	Recovered
178	1751-42	WM34	48	+	30,200	+	+	0	0	ST 68.5	6	0	13	15	0	0	Recovered
179	1789-42	CM28	24	0	cloudy	+	+	0	0	ST 15	11	0	10	15	0	0	Recovered
180	81-43	CF18	48	+	5,700	+	+	0	0	ST 118	16	0	11	13	0	0	Recovered

181	87-43	WM39	72	+	7,400	+	0	0	ST 4	ST 82	5	0	11	16	+	+	Recovered
182	92-43	WF32	48	+	8,000	?	0	0	0	ST 133	4	0	11	16	+	0	Recovered
183	95-43	WF22	36	+	13,275	+	+	0	0	ST 70	4	0	10	13	0	+	Recovered
184	117-43	WM24	24	+	8,200	+	+	+	0	ST 110	7	40,000 U	10	13	0	0	Recovered
185	143-43	WF55	24	+	55,000	+	+	+	0	ST 78	6	40,000 U	7	10	0	0	Recovered
186	232-43	CF10	48	?	3,150	+	+	+	0	ST 68	8	50,000 U	13	17	0	0	Recovered
187	284-43	WF19	72	?	24	0	+	0	0	ST 79	8	0	9	12	0	+	Recovered
188	299-43	CM 6	48	+	18,450	+	0	0	SA 4	ST 53	11	0	5	9	0	0	Recovered
189	380-43	WM15	24	+	900	0	0	0	0	ST 62	5	0	6	9	0	+	Recovered
190	518-43	WM46	72	+	35,000	0	0	0	SA ?	SA 25	17	50,000 U	3	3	0	0	Died
191	783-43	WF17	72	+	7,000	+	0	0	ST 4	ST 47	7	0	7	9	0	0	Recovered
192	290-43	WF25	48	+	17,400	+	0	0	0	ST 41 SD 5 SA 33	22	0	8	10	0	0	Recovered
193	535-43	WF1	216	0	7,500	+	0	0	0	ST 8.5	3	0	6	8	0	0	Recovered
194	242-42	WM12	48	+	27,000	+	+	+	0	SP 46	23	0	8	14	0	0	Recovered
195	395-42	WM67	96	+	10,200	+	+	+	0	SP 70.5	8	0	12	16	0	0	Recovered
196	1234-42	WF19	48	+	28,000	+	+	+	?	SP 61	—	0	9	12	0	0	Recovered
197	1350-42	WM16	72	0	22,400	+	+	0	0	SP 92.5	33	0	13	16	0	0	Recovered
198	250-42	WF23	72	0	4,500	0	0	0	0	SP 71 SD 24	9	0	8	14	0	0	Recovered
199	465-42	WF7	24	+	1,500	+	+	0	0	SP 10 SD 43	16	0	11	14	0	0	Recovered
200	1283-42	WM3	48	+	16,000	+	+	0	0	SP 7.5 SA 30 SD 21	18	0	19	21	0	+	Recovered
201	1310-42	WF28	24	+	10,250	+	0	0	SD 4	SP 44 SD 38	11	0	8	12	0	0	Recovered
202	1382-42	WM40	120	+	11,500	0	0	0	SA 4	SP 31 SA 16 SD 4	7	0	6	9	0	0	Recovered
203	1203-42	WM34	24	+	3,500	+	+	0	0	*Died before therapy could be given*							
204	1418-42	WF1.5	12	+	20	0	+	+	0	*Died before therapy could be given*							
205	2-43	WM13	12	+	58,000	+	+	0	0	*Died before therapy could be given*							
206	56-43	CF31	36	+	10,700	+	+	0	0	*Died before therapy could be given*							
207	421-43	WF7	24	0	1,500	0	+	0	0	*Died before therapy could be given*							
208	623-43	WF3mo.	24	+	350	+	+	+	35,000 U	*antimeningococcus serum*							Died
209	691-43	WM57	?	?	4,700	+	0	0	0	*Died before therapy could be given*							

The blood cultures on the latter two were sterile, but there is enough presumptive evidence to classify these as meningococcal infections.

The distribution of the number of cases among the several months covered by this report is shown in Chart VI. There is a definite predominance of cases in the early months of 1943, and a decided decline later in the year. This is the distribution that was observed in previous epidemics according to Brinton.[5]

There was no significant difference in the incidence of the disease in males as compared with females. In this series there were 113 females and 96 males.

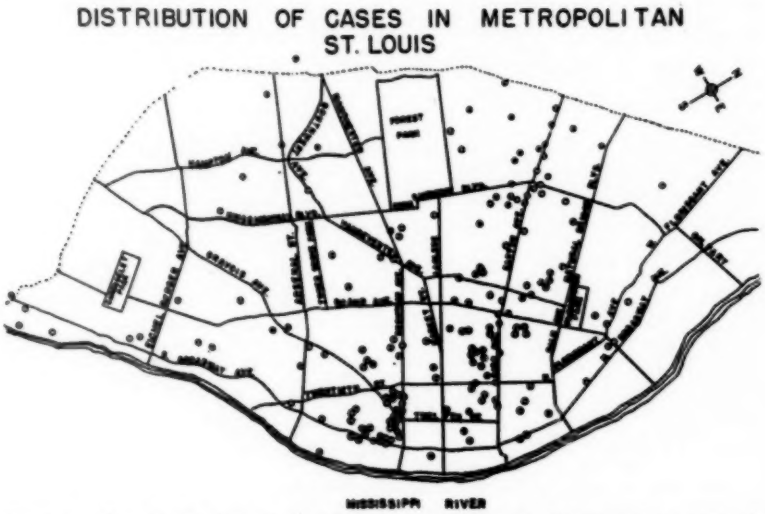

Chart V.—Map of the City of St. Louis, Mo., showing the distribution of cases of meningococcal meningitis in the 1943-1944 epidemic.

The age distribution graph (see Chart VII) is significant in that it emphasizes that the meningococcus selects principally children and young adults for its victims. The definitely greater prevalence of the disease among children (from birth to 14 years of age), as compared with adults (14 to 75 years of age) is brought out by the following figures. According to the last national census, 69 per cent of our living population was between the ages of 14 and 75, and 29.5 per cent was between the ages 0 to 14. With equal age distribution the expected number of victims between the ages of 0 to 14 should have been 64, and the expected morbidity between the ages of 14 and 75 should have been 151.8. The actual number of patients between the ages of 0 to 14 was 90, and between the ages of 14 to 75 the actual number of victims was 119.

One more observation might be pointed out. Chart VII also shows that in the age group 0 to 14, 22 patients were Negro and 69 were white. Thus 58 per cent of all infections in Negroes and 40 per cent of all infections in white people occurred in children under 14 years of age.

There seems also to be some predilection for the Negro, although there was a definite preponderance of white patients affected, 171 as compared to 38 Negro. The percentage of Negro people in St. Louis is approximately 12, and the expected morbidity for the Negro race should have been 25 in this epidemic. This figure, however, was increased by 50 per cent in the observed cases.

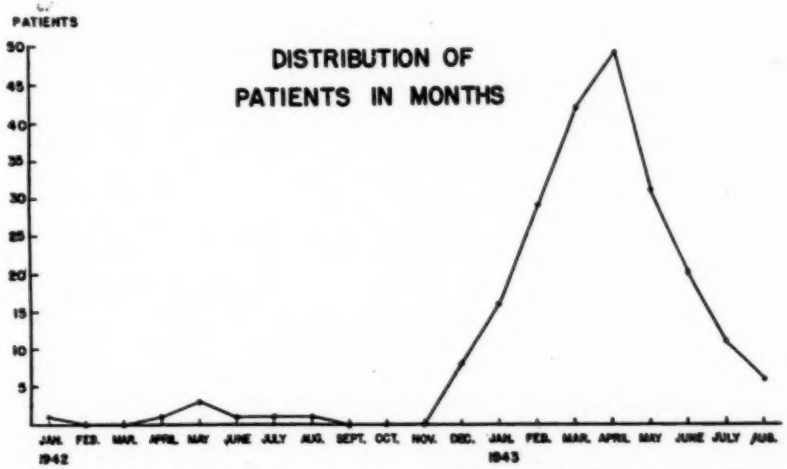

Chart VI.—Monthly incidence of cases of meningococcal infection for the years 1942-1943.

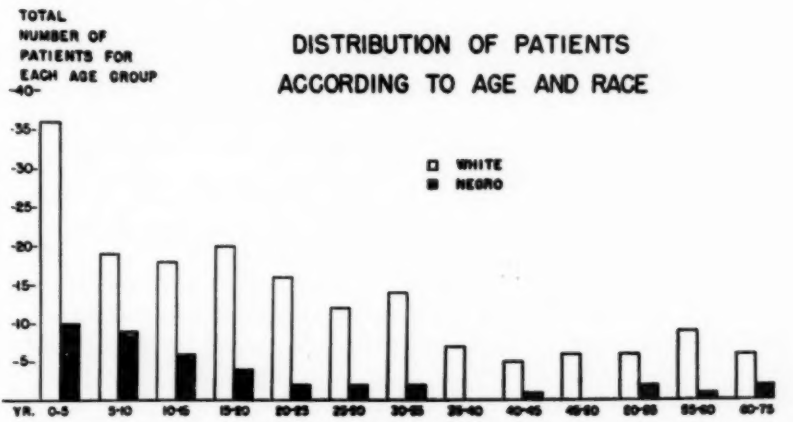

Chart VII.—Age and race distribution of cases of meningococcal infection.

It is of interest to note that 137 patients (65 per cent) in this series entered the hospital after forty-eight hours of illness. Sixty-seven patients (32 per cent) entered the hospital after three days or more of illness. Recent reports[6, 7] of meningococcic infections in certain army camps indicate a much shorter time interval between onset of symptoms and the beginning of treatment, and the case fatality rate is correspondingly lower.

Although a great number of our patients was first seen by physicians at home or at hospitals, yet very few, only 41 patients (19 per cent), received some form of sulfonamide therapy before admission to the Isolation Hospital.

The presenting symptoms in order of frequency were:

SYMPTOMS	NUMBER OF PATIENTS
Fever	196
Lethargy	173
Headache	154
Vomiting	145
Malaise	99
Chills	66
Sore throat	30
Convulsions	23

The most common signs which the patients presented were in order of frequency:

SIGNS	NUMBER OF PATIENTS
Stiff neck	200
Positive Kernig or Brudzinski signs	184
Petechiae	155

The diagnosis of meningococcic meningitis was made in all cases of demonstrated purulent meningitis in which any one of the four positive findings listed below was present.

(1) Typical petechiae
(2) Gram-negative diplococci in a stained smear of the spinal fluid
(3) Positive blood culture for *Neisseria meningococcus*
(4) Positive spinal fluid culture for *N. meningococcus.*

It might be pointed out at this time that we encountered only 6 cases of meningococcemia without meningitis. In each of these patients the typical skin rash was profuse, and the meningococcus was cultured from the patient's blood in all but two instances. These patients, B. D. (180-43) and B. W. (193-43), were admitted from a one-room dwelling in which another proved meningococcic infection originated within a week, and we felt justified in making a diagnosis on the basis of a typical rash without positive blood culture.

The length of hospital stay ranged from six to forty-two days for those patients who recovered. The average duration of hospitalization was 12.8 days. There were no definite criteria for discharge, the patient being signed out after he had been off chemotherapy for several days and appeared to be well clinically. There have been no known relapses among the discharged patients.

MANAGEMENT AND THERAPY OF PATIENTS

Although there were slight variations in the management and therapy of patients at the inception of the epidemic, the plan of treatment had assumed a uniform pattern when the disease had reached epidemic proportions, and the following is a résumé of the routine employed.

In addition to the usual information obtained in the medical history of each patient, specific questions were asked about the duration of illness before entry to the hospital, whether any chemotherapy was given before admission, and about the following symptoms: fever, headache, vomiting, chills, lethargy, sore throat, muscular aches and pains, and convulsions. During the physical examination special attention was paid to the following signs: petechiae, stiff neck, Kernig and Brudzinski signs, and evidence of collapse.

Certain laboratory procedures and diagnostic tests were used routinely. Most patients included in this series had a lumbar puncture upon admission to this hospital. The only exceptions were the few patients who had lumbar punctures performed in the hospitals from which they were transferred. In these cases the information gained from a spinal fluid examination was obtained from the private physician or the referring hospital.

Additional lumbar punctures during the patient's stay in the hospital were performed only when the response to treatment was not satisfactory; that is, when fever persisted for more than a few days after admission, when there occurred a sudden temperature elevation, or when the signs of meningeal irritation persisted past the third day of treatment. The spinal fluid was examined at once for cellular content, for organisms by stained smear, and was cultured* using the candle method for obtaining micro-aerophilic conditions. Blood cultures were secured on all patients upon admission and thereafter in most instances when the temperature rose suddenly to more than 103° F.

Adequate hydration of the patients during active chemotherapy was stressed; all adults received from 3,000 c.c. to 5,000 c.c. of fluids daily, and children received at least 10 per cent of the body weight in fluids per day. The parenteral route was relied upon for the administration of fluids during the first two or three hospital days until the patient could take and retain liquids easily by mouth. The parenteral fluids used were 10 per cent glucose for intravenous administration and some type of lactate—Ringer's solution for subcutaneous use. An effort was made to keep an accurate record of each patient's fluid intake and output.

Six sulfonamide drugs were used in the treatment of the patients in this series. These were sulfadiazine† (2-*p*-aminobenzene sulfonamidopyrimidine), sulfamerazine (2-sulfanilamido-4-methylpyrimidine), sulfa-

*The culture medium used was horse meat broth agar, containing bacto-peptone, human blood (8 to 10 per cent), para-aminobenzoic acid (5 mg. per 100 c.c.). This was prepared according to the method of H. D. Wright (J. Path. & Bact. 37: 257, 1933).

†Sulfadiazine for this study was supplied through the courtesy of Major Joseph C. Edwards, Medical Corps, Army of the United States, and Lederle Laboratories, Inc.

pyrazine (2-sulfanilamidopyrazine), sulfapyridine (2-*p*-sulfanilamidopyridine), sulfathiazole (2-*p*-aminobenzene sulfonamidothiazole), and sulfanilamide (*p*-aminobenzene sulfonamide).

A number of patients received sulfonamide chemotherapy before admission, and we continued therapy with the same drug whenever this seemed practical and for the patient's best interest. Sulfadiazine was the principal drug used in the management of 110 patients. Thirty-six patients were treated with sulfamerazine and represented part of a study of this new drug undertaken by members of the Washington University Department of Internal Medicine.[2] Twenty-three patients treated with sulfapyrazine were all children and were part of a study of sulfapyrazine undertaken by members of the Department of Pediatrics[3] of Washington University. Only 9 patients were treated with sulfapyridine. The 15 individuals who received sulfathiazole were carefully selected and included only those patients who presented typical clinical and laboratory findings of meningococcic meningitis and who were not desperately ill. Patients treated with sulfanilamide usually represented those who had developed urinary tract complications during the course of therapy with one of the other sulfonamide drugs.

The plan of chemotherapy was essentially as follows: Every patient with meningitis that was admitted to this hospital was treated as though he had one of the most serious forms of meningitis; that is, pneumococcal or influenzal. During the first twenty-four or forty-eight hours all patients received sulfonamide drug in quantities adequate to cope with such serious infections. It was not until the causative organism was grown out in culture and shown to be a meningococcus or until the clinical course clearly pointed to a meningococcic infection that the intensive chemotherapy was reduced. The following is the pattern of drug administration that was followed in most cases.

For adults 15 Gm. of the sodium salt of a sulfonamide were given subcutaneously in the first twenty-four hours, and for children the initial twenty-four-hour dose was calculated on the basis of from 0.4 to 0.5 Gm. per kilogram of body weight. This calculated dose was usually divided into three equal parts, one-third being administered immediately, and the remaining two-thirds given in two equal doses at eight-hour intervals. The sodium salts were given in ½ per cent concentration in a "fortified lactate-Ringer's" solution. Most patients received an additional intravenous injection of 10 per cent glucose, 750 c.c. for adults and a proportionate amount for children. By such a regimen adequate fluid intake, adequate and accurate administration of sulfonamide, and a dilute alkaline urine were assured.

The second and third twenty-four-hour period of therapy were usually much less standardized and consisted simply of maintaining the 20 to 40 mg. per cent level of drug in the blood with sufficient fluids and alkali to maintain a large volume of alkaline urine. As soon as the

patient became sufficiently rational and cooperative, usually within the second period of twenty-four hours, drug and fluids were begun orally. The initial intensive chemotherapy was relaxed as soon as definite clinical improvement was apparent. Adults were usually dropped from 15 Gm. per twenty-four hours to 12 Gm., then to 8 Gm., and maintained on 8 Gm. daily for about five days. In children when the temperature was normal for two days, the drug dosage was reduced to 0.2 Gm. for 1 or 2 days, then to 0.1 Gm. per kilogram per twenty-four hours, and after two more days of normal temperature, drug administration was discontinued. The average number of days that all patients in this series were treated with sulfonamides was 8.9 days.

Sulfonamide levels of the blood and spinal fluid were obtained every day on those patients who were treated with sulfamerazine and sulfapyrazine, and the findings have beeen published elsewhere.[8, 3]

In those patients receiving the other sulfonamides, drug levels of the blood were secured every other day, and spinal fluid levels were obtained whenever lumbar puncture was done.

Thirty-six patients in this series received antimeningococcal serum.* The antiserum was given only to those patients who were in shock or were moribund in the admitting room, usually from fulminating meningococcemia. Adults were given from 40,000 to 60,000 units and children from 20,000 to 30,000 units, one-half intravenously and the remainder, intramuscularly. Such patients were given, in addition to chemotherapy and antiserum, adrenal cortex hormone, intravenous glucose, oxygen, adrenalin, and other stimulants.

COMPLICATIONS

Fortunately there were few serious complications observed during this epidemic. Arthritis was one of the most common and was noted in 20 cases (9.5 per cent). Only the joints of the extremities were involved, and in each instance more than one joint was affected. Arthritis was noted both early and late in the course of the disease, and it was not unusual to have the disability develop while the patient was receiving sulfonamide treatment. Most of the affected joints showed tenderness, swelling, increased heat, redness, and limitation of motion. Very few patients developed a frankly purulent arthritis, and when pus was aspirated it was always found to be sterile. No permanent residual disability was seen in any of the patients.

There were 6 cases (2.9 per cent) of bilateral deafness. All of these patients were unconscious and gravely ill for the first few hospital days, so that the deafness was not apparent until convalescence had begun. It was our impression that the deafness was total, although no accurate analysis of the degree of deafness was made. In no instance had the hearing improved at the time of discharge, and these patients have not been followed since leaving the hospital.

*Lederle Laboratories, Inc.

There was noted in one patient a peripheral facial palsy and foot drop. Both palsies had disappeared before the patient's discharge from the hospital. In another patient a gross tremor appeared that was limited to the upper extremities, and the tremor was still present at the end of the hospital stay. Four patients had one or more generalized convulsions late in their convalescence. These were the first convulsive episodes known to the patients or their relatives. There was a family history of epilepsy in only one of these individuals. It was impossible to follow these patients after discharge, but at the last examination they presented no abnormal findings.

One individual was admitted with a bilateral metastatic panophthalmitis and was partially blind. At the time of discharge vision had returned, and the eyes appeared quite normal.

COMPLICATIONS OF SULFONAMIDE THERAPY

Twenty-seven unfavorable reactions to sulfonamide drugs were recorded, an incidence of 13.3 per cent in the 202 patients receiving chemotherapy. Only two of these reactions occurred in patients who died, and in only one instance was the sulfonamide a possible factor in the fatal outcome. This was the case of a 52-year-old white male who responded very poorly to sulfamerazine and finally developed pneumonia after two weeks of sulfamerazine therapy with blood levels varying between 12 and 25 mg. per cent. Because he developed pneumonia while on sulfamerazine, it was decided to change to sulfapyridine, and the patient died after four days on this latter drug. At autopsy there were concretions in the kidneys and ureters with evidence of obstruction of the urinary tract. The concretions obtained at autopsy were analyzed* and were found to be composed of acetylsulfamerazine.

Another serious complication was seen in the series, but the patient recovered. This was an instance of agranulocytosis that developed in a patient receiving sulfadiazine. A single instance of mental confusion due to sulfapyridine was noted. Four patients developed uncomplicated morbilliform rashes that were not of serious consequence. Five instances of drug fever were recorded.

The most common complication of sulfonamide therapy was gross hematuria, which occurred 15 times, an incidence of 7.4 per cent. Microscopic hematuria was noted in an additional 15 instances. There were 2 patients with hematuria who had associated abdominal pain that was interpreted as being due to ureteral obstruction and spasm. The following table indicates the percentage of hematuria occurring with the various sulfonamides.

DRUG	NUMBER OF PATIENTS	GROSS HEMATURIA	MICROSCOPIC HEMATURIA	PERCENTAGE OF GROSS HEMATURIA
Sulfadiazine	110	10	9	9.0
Sulfamerazine	36	3	1	8.3
Sulfapyrazine	23	2	0	8.7
Sulfathiazole	15	0	0	0.0
Sulfapyridine	9	0	5	0.0

*The chemical analyses were carried out in the laboratories of Sharp & Dohme, Inc., Glenolden, Pennsylvania.

Too much weight should not be given these figures, because as has already been pointed out, the cases were selected for the different drugs. Therapy with sulfathiazole, for example, was never very intensive because the less seriously ill patients were given this sulfonamide. The early cases given sulfamerazine were carefully chosen also because for a time the sodium salt was not available for parenteral use.

FATALITIES

Before a statement is made about the case fatality rate in this series, certain factors which directly influenced it should be stressed.

(1) Both extremes in age were represented. The youngest patient was 3 months of age and the oldest, 80 years of age. Nineteen patients seen in this epidemic were under 2 years of age, and 6 were under 1 year of age. Thirty-seven patients were 40 years of age or over. Twenty-four patients were 50 years or over, and 7 persons were over 60 years of age.

(2) Although 78 of the patients in this series entered the hospital during the first twenty-four hours of illness, 98 patients entered for treatment after two days of illness. Thirty-one patients entered the hospital after four or more days of illness.

(3) Very few patients (41) in this series received sulfonamide therapy before entry into the hospital, and in most of these cases the therapy was inadequate.

The total number of deaths in this series was 19, which represents a 9.1 per cent case fatality rate. Ten patients died within twenty-four hours after admission. These patients died either before any therapy was given or received only a minimal amount of sulfonamide drug. If we deduct this number from the total of 19, we then have a corrected mortality rate of 4.5 per cent.

Among the 9 patients who survived for more than twenty-four hours but eventually died, 5 were 60 years of age or over, and 3 were 45 years or over. As already noted, one of these patients probably died from the toxic complications of sulfonamide chemotherapy one week after the meningitic process was cured and while he was being treated for a bronchopneumonia which developed in the wake of his initial illness.

AUTOPSY FINDINGS

Post-mortem examinations were allowed on 10 patients. The findings were not unusual. There were 2 patients, H. H. (56-43) and R. T. (1418-42), who showed extensive hemorrhage into the adrenal glands. Both of these patients had a fulminating type of meningococcemia. Two patients showed acute pulmonary edema, J. S. (2-43) and J. M. (309-43). The other autopsies revealed only the evidence of purulent meningitis.

COMMENT

In reviewing our experiences during this epidemic, we were impressed with the importance of instituting immediate, intensive parenteral chemotherapy as soon as a definite diagnosis of purulent meningitis was made.

Earliest possible therapy is important because of the rapid fulminating course taken by some forms of this disease. We have seen a number of patients die within from twelve to twenty-four hours after the onset of symptoms.

Initial intensive therapy is of importance because at first inspection of a patient with meningococcal infection it is impossible to predict how severe the illness will be. Since the optimum in vivo bacteriostatic sulfonamide drug level effective against the meningococcus has not been established definitely, we believe it is best to obtain levels which are certain to be effective against this organism. We consider this level to be between 20 to 40 mg. per cent.

A second point in favor of intensive chemotherapy in the treatment of meningococcal meningitis is that frequently the recovery of the meningococcus is delayed for one or more days, and a patient thought to be infected with the meningococcus is later found to have a purulent meningitis due to the pneumococcus or influenzal organisms. The levels of drug we strived to attain; that is, 20 to 40 mg. per cent would, therefore, be considered adequate to cope with any of these infections.

The parenteral route of administration of the drugs was depended upon since we could place little reliance on drugs given by mouth to be retained, as many of the patients were vomiting during the first one to two days of their illness.

The intravenous route of sulfonamide administration was abandoned in favor of the subcutaneous method of administration, although the former method is quite good if the patient is not dehydrated. It seemed most satisfactory to us to give the sulfonamide drugs subcutaneously in ½ per cent solution. The sodium salt thus diluted was found to be nonirritating to the tissues, and hydration of the patient was accomplished concurrently, and adequate blood levels usually were attained in from two to three hours.

SUMMARY AND CONCLUSIONS

1. Two hundred and nine patients with meningococcic infections were admitted to the St. Louis Isolation Hospital between January of 1942 and August of 1943. The majority of cases was seen in the first six months of 1943.

2. A predilection of the disease for younger individuals and for Negroes was noted. There was a fairly equal distribution between the sexes.

3. Classical signs of meningitis or meningococcemia were present in the majority of patients. Petechiae were noted in 155 instances.

4. The diagnosis of meningococcal infection was based on the recovery of the meningococcus from blood or spinal fluid or on the discovery of typical petechiae in patients with purulent but sterile spinal fluid.

5. A regimen of rather intensive sulfonamide chemotherapy was used with satisfactory results. It is felt that the optimum blood sulfonamide level is between 20 and 40 mg. per cent until the patient shows definite clinical improvement. No unusual evidence of harm to patients from these blood levels was noted. A large volume of dilute alkaline urine is thought to be important in preventing hematuria. Sulfanilamide may be used to replace other sulfonamides in the treatment of meningococcic infections if gross hematuria or suppression of urine occurs.

6. The newer sulfonamides, sulfamerazine and sulfapyrazine, appear to be as effective as sulfadiazine in controlling meningococcic infections. For careful clinical studies of these drugs, the reader is referred to earlier reports in the medical literature.

7. The case fatality rate in this group of patients was 9.1 per cent. One-half of the deaths occurred in patients who were moribund on admission. If these deaths are excluded, the case fatality rate is 4.5 per cent. The majority of deaths in patients who survived over twenty-four hours after admission to the hospital occurred in elderly individuals.

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INTRADERMAL USE OF CONVALESCENT SERUM AGAINST MEASLES

Preliminary Report

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MEASLES remains one of the most serious infections seen today not only in children but also in young adults. Methods of prevention and attenuation have consisted chiefly in the intramuscular injections of convalescent serum and placental globulin extract within a few days after exposure. This immunization has been considered to be passive and short-lived, but this view, in light of the number of individuals who have been protected and fail to develop the infection on re-exposure in following epidemics, should be re-examined.

The purpose of this study is to call attention to a new method of protection against measles with recent convalescent measles serum. The results suggest that active immunity has been acquired by the inoculated individuals.

The epidemic of measles invading Houston in 1944 was quite widespread and severe. Many children developed the infection and had extremely high fever with a number of complications. With the onset of the epidemic there was sufficient placental extract to give all contacts desiring inoculation, but the supply diminished and ceased two-thirds of the way through the epidemic. At this point the opportunity presented itself of obtaining serum from two adults just recovering from an attack of measles and this study is a report on the use of this sera intradermally in a group of exposed children and adults.

THE SERA

The serum from one adult was obtained three days after the temperature was normal and the rash was still present. The serum from the second adult was obtained one week after the temperature was normal. The serum was not pooled but placed in 10 c.c. amounts in rubber-covered 20 c.c. glass bottles. The serum was frozen and thawed for use when required.

DOSAGE

Each child was given, regardless of age, 0.4 c.c. intradermally in daily doses for five doses, the total serum received intradermally being 2 c.c.

RESULTS

Forty individuals, two adults and thirty-eight children, intimately exposed to measles either in the immediate family, or in chauffeur

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TABLE I

AGE GROUPS	TIME OF IMMUNIZATION AFTER EXPOSURE	CASES (NO.)	MEASLES	REMARKS
6 mo. to 2 yr.	0 to 4 days	3	0	
	4 to 8 days	5	0	
	over 8 days	1	0	
2 yr. to 6 yr.	0 to 4 days	4	2	Attenuated measles at 14 days
	4 to 8 days	9	0	
	over 8 days	2	0	
6 yr. to 10 yr.	0 to 4 days	4	1	After 4th inoculation
	4 to 8 days	5	1	After 4th inoculation
	over 8 days	2	0	(Both uncomplicated measles)
10 yr. to 15 yr.	0 to 4 days	1	0	
	4 to 8 days	2	0	
	over 8 days	0	0	
15 yr. and over	0 to 4 days	1	0	
	4 to 8 days	0	0	
	over 8 days	1	0	
Total		40	4	

groups, received the recent convalescent sera in 2 c.c. amounts intradermally. The results are shown in Table I.

Two children developed measles after the fourth inoculation. Both of these children developed severe measles with no complications. Two children, twin girls, J. and P., developed extremely mild measles fourteen days after the start of the inoculations. The sister to whom they were exposed had a very severe measles infection with temperature up to 106° F. for several days, and eventually developing a bronchopneumonia and otitis media. J. and P. did not develop fever over 103° F., and the fever lasted but three days. They had little cough and their rash lasted three days. The remaining thirty-four children and two adults remained free of infection.

There were no reactions to any of the inoculations with the exception of one child who developed a slight urticarial local reaction on the first and second injection. This urticarial reaction was approximately 2 by 3 cm. each time.

COMMENT

The small doses of sera given and the extremely high degree of protection received in this group of children lead one to believe that the immunity so produced is that of an active character. A further report will be given when these children are exposed to succeeding waves of epidemics.

Economically this method of protection with 2 c.c. of convalescent serum has much to commend it over the use of from 20 to 30 c.c. given intramuscularly in the past. And at least ten times the number of children can be immunized with the same amount of serum.

There were no reactions with the exception of the urticarial responses in one girl on the first and second injections. No local discomfort was

observed as compared to that occasionally seen when a volume of from 20 to 30 c.c. of convalescent serum was used intramuscularly.

Stillerman and Thalhimer[1] stated that the secondary attack rate of measles in intimately exposed susceptible family contacts, 1 month to 14 years of age, observed in the 1941 epidemic in New York City was 75 per cent. In this group of forty individuals exposed intimately to measles, thirty would have been expected to develop the disease. Instead two developed an unattenuated infection not having time to complete the injections and two developed an attenuated infection fourteen days after the inoculations.

Dungal[2] observed a rate of protection of 70 per cent in 203 persons receiving convalescent serum intramuscularly during the 1943 epidemic in Iceland. He made the interesting observation that of 45 individuals developing the infection after inoculation, 16 were affected within ten days after the injection, 15 were affected between ten and thirty days, 3 were affected between the thirtieth and fiftieth days, and 11 were affected after fifty days had passed. Assuming that the immunity produced by the sera that was given intramuscularly resulted in a passive immunity, then the greatest degree of protection or immunity would be thought to occur shortly after the sera was given and this immunity to taper off gradually due to passive loss of serum and antibodies from the injected individual. The curve of incidence of individuals developing measles is almost exactly the reverse of the curve of the titer seen in a passive immunity. That is to state that protection does not parallel the maximum titer of the passive immunity but is in line with the curve of resistance produced by an active immunity.

Stillerman and Thalhimer[1] made another interesting observation that there is no significant difference in the rate of protection obtained for contacts of any dosage group given injections from four to seven days after exposure, but on the eighth day the rate of protection decreased sharply, although modified measles occurred in the remainder not completely protected. This is suggestive that an active immunity was produced to some extent by the intramuscular injections, the degree of active immunity produced had definite values the ceiling of which was not changed by an excess of serum, and the active immunity is complete only if sufficient time is allowed before the invasion of the disease. If sufficient time is not allowed for active immunity to develop fully then only a partial immunity is conferred and attenuated measles results.

In the present series it is difficult to see how passive immunity was conferred by 2 c.c. amounts intradermally. The protection developed in such a high percentage of contacts as in this series must have been of an active character, and the intradermal layer of the skin furnished an excellent means for producing this immunity. Apparent immunity was also produced in some of seven persons on the eighth day or longer after exposure to the disease, for they did not develop the infection.

It is thought that in the serum of recent convalescent measles patients within a week after cessation of fever and rash there occurs sufficient attenuated virus acting as an antigen to produce a potent active immunity when this serum is given intradermally in the amounts suggested. The duration of this immunity is not known at the present time.

The length of time this serum can be stored and still retain its value is not known. Bull[3] stated that serum stored for nearly three years seemed quite as effective as that collected six months before use in prophylaxis of measles. The serum used in the present series contained no preservative, and it remains to be seen if the antigenic value survives long periods of freezing.

SUMMARY

1. Forty persons, two adults and thirty-eight children, have been given recent convalescent measles serum intradermally.

2. The serum was given in 0.4 c.c. amounts intradermally on successive days until 2 c.c. were given.

3. Thirty-four children and two adults did not develop measles. Two children developed uncomplicated measles before the course was completed. Two children developed attenuated measles fourteen days after the inoculations.

4. It is believed at the present time that recent convalescent measles serum has enough measles antigen available to produce an active immunity when this serum is given intradermally in at least the amounts suggested.

5. The intradermal employment of recent convalescent measles serum in the amounts suggested provides an economical use of this product.

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GENERALIZED OBSTRUCTIVE EMPHYSEMA IN INFANTS

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ACUTE and chronic respiratory disturbances in which the characteristic clinical manifestation is an expiratory type of dyspnea associated with generalized emphysema are not uncommon in the first few years of life. While from a clinical standpoint the cases which fall in this category have certain features in common, they do not represent a single entity. Etiologically they vary to a considerable extent. In certain instances the history, associated clinical features, and laboratory tests may provide a clue to the etiology, but in others only an inferential diagnosis is possible and the actual cause is established only at autopsy, if at all.

The respiratory obstruction is principally in the distal or smaller bronchioles, and clinically such diagnostic terms are employed as "bronchiolitis," "capillary bronchitis," "pneumonitis," "interstitial pneumonia," and in certain instances "aspiration pneumonia." There is, as a rule, obstruction to both inspiration and expiration, but the difficulty in expiration is the more prominent and air is trapped in the alveoli producing emphysema. There are, of course, marked variations in the degree of obstruction as well as in the nature of the obstructing lesion, so that not only does the degree of emphysema vary, but in the same case there are frequently areas of atelectasis as well as of emphysema. Atelectasis naturally follows the emphysema when the obstruction is complete and the trapped alveolar air has been absorbed. Clinically there are certain similarities to asthma, but in contrast to the usual relatively short duration and self-limited course of the average attack of asthma, even the acute forms of obstructive emphysema in infants tend to persist for a week or so and many of them for a much longer period of time. Furthermore, while asthma is perhaps the most frequent cause of obstructive emphysema in older children, it is relatively uncommon in the first year or two of life, when the conditions under consideration characteristically occur.

While no single description is applicable to all cases of obstructive emphysema, there are certain features which they have in common. There are an increased respiratory rate and markedly decreased respiratory excursions associated with a utilization of the accessory muscles of respiration. This latter results in an indrawing at the suprasternal notch and at the lower margin of the thorax. The indrawing at the upper and lower ends of the sternum and of the thorax is not so marked as in severe laryngeal or tracheal block where the obstruction is principally inspiratory in type. In contrast to laryngeal obstruction, there

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is usually no hoarseness or stridor and in contrast to asthma, frequently no audible wheezing. Cyanosis depends upon the degree of the obstruction. The percussion note is hyperresonant except over localized areas of consolidation, and the respiratory murmur is characterized by a prolongation and usually a roughening of the expiratory phase. There may or may not be fine or medium râles. Roentgenographic and fluoroscopic examinations of the chest are of great help in confirming the diagnosis. On the roentgenogram, the diaphragm is seen to be low and flattened, the ribs farther apart than usual, and the lung fields less dense. There may or may not be stringy or patchy areas of density or even relatively large areas of atelectasis. Of even more significance, however, is the fluoroscopic evidence of the markedly restricted excursion of the low and flattened diaphragm. In the more severe cases the excursion is so slight that it appears to be little more than a quivering movement. Furthermore, there may be a slight increase in the horizontal diameters of the chest during expiration suggesting that the emphysematous lungs are simply being forced into a different position rather than being emptied of any significant quantity of the trapped air.

In our experience this type of respiratory disturbance is far from uncommon and, while the majority of the infants observed have had an acute, self-limited course, unaffected by the sulfonamides, and strongly suggestive of being the infantile counterpart of influenzal (virus) pneumonitis or of so-called primary atypical or viral pneumonia, there has been a variety of pathologic conditions which have been responsible for dyspnea in association with obstructive emphysema. These have included aspiration of amniotic contents during birth, cystic fibrosis of the pancreas, atypical bronchopneumonia, laryngotracheobronchitis, miliary tuberculosis, aspiration of zinc stearate powder, and chronic passive congestion secondary to a congenital heart lesion.

The following case histories* illustrate conditions in which obstructive emphysema is an important feature.

ASPIRATION OF AMNIOTIC CONTENTS

CASE 1.—Infant G., male, was born Oct. 9, 1941, and died Oct. 11, 1941. He was a full-term infant, the mother a primipara, with medical induction of labor. Sodium pentothal anesthesia was used. Low forceps delivery took place after labor of 12 hours. The membrane ruptured at delivery; the amniotic fluid contained a large amount of meconium.

The weight of the infant was 7 pounds, 11 ounces; the length, 20½ inches. Resuscitation was difficult, thick yellow mucus was aspirated from the pharynx, respirations were irregular, and there were frequent attacks of apnea. The skin was covered with a dirty greenish yellow material. The color of the skin was ashen gray but was improved somewhat by oxygen; the cry was weak; the chest contained many

*The infants whose histories are cited were patients either of the Pediatric or Bronchoscopic Departments of Temple University Hospital, and all of the infants were seen by members of both departments.

coarse râles, and the heart sounds were of average quality. There were 6,250,000 red blood cells and the hemoglobin was 21 Gm. per cent. During the two days of life, the respiratory difficulty increased, and on auscultation there were many crepitant râles, and only a limited exchange of air. Bronchoscopic aspiration was considered but decided against because obstruction seemed to be in the periphery. Death occurred during one of the periods of apnea.

Pathologic Report

Gross Findings.—(The right lung weighed 48 Gm. and the left, 40 Gm.) The lungs presented identical findings. Patchy areas of atelectasis were seen over all lobes as bluish red areas depressed below the surrounding surface. These were devoid of any crepitation and had a rubbery consistency. Sections of the lungs confirmed the presence of the atelectatic areas. In addition, there were innumerable tiny nodules

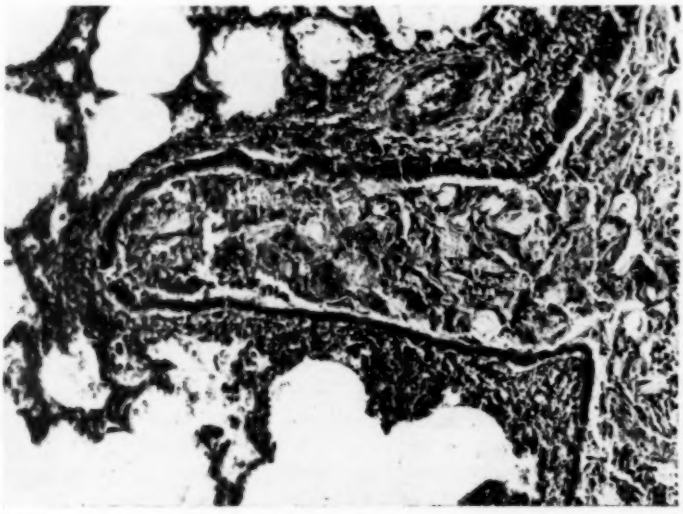

Fig. 1 (Case 1).—Small bronchus filled with meconium and precipitated amniotic fluid. Note dilatation of alveoli in adjacent lung field.

of a peculiar faint greenish yellow hue which were diffusely distributed over the entire periphery of the lung. Yellowish green exudate was also present in many of the smaller bronchioles.

Microscopic Findings.—This case represented a rather fulminating instance of aspiration pneumonia in the newborn infant. Not only was amniotic fluid present in many areas in rather large amounts but what appeared to be actual meconium was found as casts filling many of the larger and medium-sized bronchi and in some instances was traceable in direct continuity to the smaller bronchioles (Fig. 1). In a few areas the meconium was found in the alveolar spaces but, for the most part, the material in the lung parenchyma itself represented a precipitated hyaline-like substance presumably from the amniotic fluid. This tended to be demonstrable as a film of varying thickness over the alveolar walls. (Fig. 2). Dilatation of these alveoli with a striking emphysema was

noted. This emphysematous process was extremely patchy but very widespread. There was very little cellular reaction; in some areas there was beginning polynuclear infiltration but the mechanism of death was mechanical inhalation of material with blocking of the bronchial tree rather than a true inflammatory exudative phenomenon as the cause of the obstruction.

CASE 2.—W. G., male infant, was 5 months of age. The birth weight was 6 pounds. The birth was two weeks premature after a "dry labor" of about five hours. Membranes had ruptured about four or five days before delivery. Respiratory difficulty was present from the time of birth. During the first ten weeks of life there were several attacks of apnea and cyanosis. Roentgenograms of the chest during this period showed a shifting atelectasis and bilateral emphysema.

The respiratory difficulty continued with a decreasing tempo and when he was seen at 5 months of age his weight was 13 pounds, 6

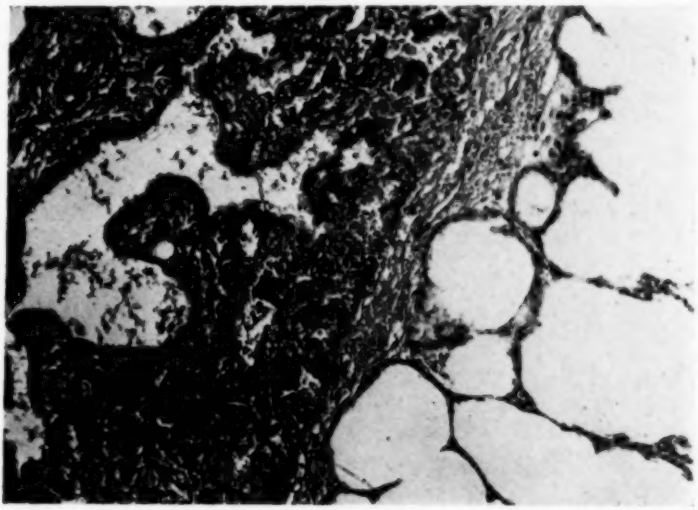

Fig. 2 (Case 1).—Section through interlobular septum. Note the typical hyaline "asphyxial membrane" outlining dilated alveoli and accompanied by pneumonic cellular infiltration in the one lobule and with marked emphysematous airsacs in the other.

ounces, and his general condition was fairly good. Respirations were characterized by inspiratory supra- and substernal retractions and by an occasional stridor. The chest was hyperresonant, the breath sounds were roughened, and there were occasional clicking noises but no moist râles. Roentgenograms of the chest showed rather marked bilateral emphysema and disappearance of the gross atelectasis, but some stringy densities remained.

Impression.—The impression was bilateral obstructive emphysema with some residual atelectasis. The most likely explanation appeared to be residual damage from aspiration of amniotic fluid during labor.

CASE 3.—W. I., white male infant, 5 months of age, was admitted to the hospital March 30, 1944, and dismissed April 27, 1944. The mother had intermittent labor pains for one week prior to delivery. The in-

tervals were said to be as short as from five to ten minutes on some days and the pains quite severe. She thought that the fetus became somewhat less active during this period. The actual labor lasted about three and one-half hours. The membranes were ruptured just before the baby was delivered so that fluid was being expelled while the baby was passing through the birth canal. The mother had no knowledge of any respiratory difficulty during the seven-day period in the hospital, but she noted that the baby's breathing was noisy on arrival at home. On the third day at home it was thought that he had a "cold" and indrawing was noted in the suprasternal and lower costal areas during respiration. Subsequently there were several respiratory infections characterized by increased dyspnea and by cyanosis; several weeks before admission the infant had an attack of bronchopneumonia. The difficulty in breathing continued during the periods of remission from active respiratory infection. At the time of admission there was no fever or cyanosis, but there was an indrawing of the supra- and substernal areas with inspiration. The chest was resonant to hyperresonant, expiration was prolonged and roughened, and fine crackling râles were heard over the left lung. During the stay in the hospital there were several acute exacerbations of the respiratory symptoms with fever. At these times it was necessary to place the infant in an oxygen tent although this was not otherwise necessary. Fluoroscopic and roentgenographic examinations revealed marked obstructive emphysema which was not relieved by the administration of epinephrine. Intracutaneous tuberculin tests were negative. Although the stools appeared normal, a duodenal aspiration was performed. The aspirated contents showed a normal trypsin content which was interpreted as evidence against the diagnosis of cystic fibrosis of the pancreas. Bronchoscopic examination did not disclose evidence of a laryngotracheitis.

Impression.—While an etiologic diagnosis was not possible, it was thought that this infant had a chronic bronchiolitic infection which may have been superimposed upon injury resulting from amniotic aspiration or which had simply followed an initial bronchiolitis, the acute episodes being due to exacerbations of the chronic infection or to superimposed acute infections.

Comment

There can be no doubt that the respiratory difficulty in the first case was due to the obstruction of the entire bronchial tree as well as of the alveoli. Death was apparently due to asphyxia and to the exhaustion resulting from attempts to combat it. An absolute diagnosis is not possible in Cases 2 and 3, but by exclusion of other causes and by inference, it would seem that the respiratory difficulty stemmed from the initial obstruction caused by aspiration of fluid and other material from the birth canal in Case 2 and possibly so in Case 3. It is probable that some amniotic fluid is aspirated by all infants during the process of birth, but in most instances the amount is sufficiently small that no significant disturbance is produced. The question is whether there are instances in which aspiration is sufficient to cause respiratory obstruction with more or less permanent residual lung changes but without causing death. This would appear to be a possibility.

CYSTIC FIBROSIS OF THE PANCREAS

CASE 4.—S. E. H., female infant, 3 months of age, died after nine days in the hospital. At 3 weeks of age, the infant developed pneumonia and was hospitalized elsewhere for a period of three weeks. One week after apparent recovery, she was returned to the hospital with another severe respiratory infection. When transferred to Temple University Hospital, she appeared moribund. She was cyanotic, the respirations were irregular and gasping, and there was some retraction of the lower costal cage. On auscultation, an expiratory wheeze and numerous coarse râles were heard. Roentgenographic and fluoroscopic examinations of the chest revealed obstructive emphysema of both lungs with accentuation of the perihilar and peribronchial markings. The leaves of the diaphragm were flattened and the movements were limited and jerky. The infant received oxygen continuously, sulfathiazole, blood transfusions, and several bronchoscopic aspirations. Culture of the aspirated material revealed *Staphylococcus aureus, Hemophilus*

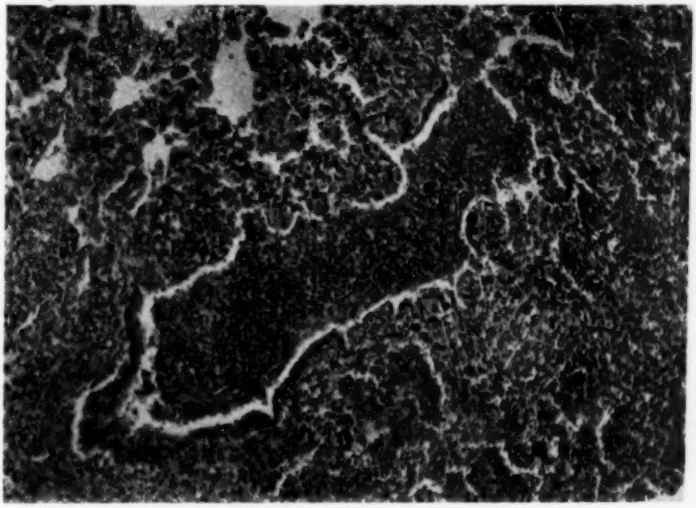

Fig. 3. (Case 4).—Terminal bronchiole and atrium filled with acute suppurative exudate, extending into lung parenchyma as a diffuse bronchopneumonia.

influenzae, and a bacillus resembling the Friedländer group of organisms. Since the stools were bulky, although there was no offensive odor, fat analysis was obtained. Total fats, soaps, and fatty acids were 64 per cent of the weight of the dried stool. Death was due to respiratory infection and obstruction.

Impression.—The impression was chronic diffuse pulmonary infection (chronic bronchiolitis or interstitial pneumonia) secondary to cystic fibrosis of the pancreas.

Pathologic Report

Gross Findings.—(The left lung weighed 47 Gm. and the right, 45 Gm.) The trachea and main bronchi were partially filled with a thick, sticky, mucinous, suppurative exudate. There were numerous areas of atelectasis scattered over the surfaces of both lungs with one especially

prominent area on the anterior border of the upper right lobe. There were smaller areas in both lungs which were especially prominent along the posterior borders. Throughout the left lower lobe there were numerous pea-sized nodules of consolidation. When sectioned, the parenchyma had the mottled appearance of patchy bronchopneumonia. The pleura was normal in appearance. Grossly, the pancreas showed no changes of diagnostic significance.

Microscopic Findings.—The sections presented a somewhat complex picture with evidence of both chronic inflammation of the medium and larger-sized bronchi and of terminal acute superimposed suppurative bronchitis and bronchiolitis with secondary extension to the alveoli producing a patchy bronchopneumonia. The medium-sized and larger bronchi showed some inflammatory hyperplasia of their lining cells with plication, but there were no loss of cilia and no evidence of actual squamous metaplasia. The peribronchial tissues were edematous and

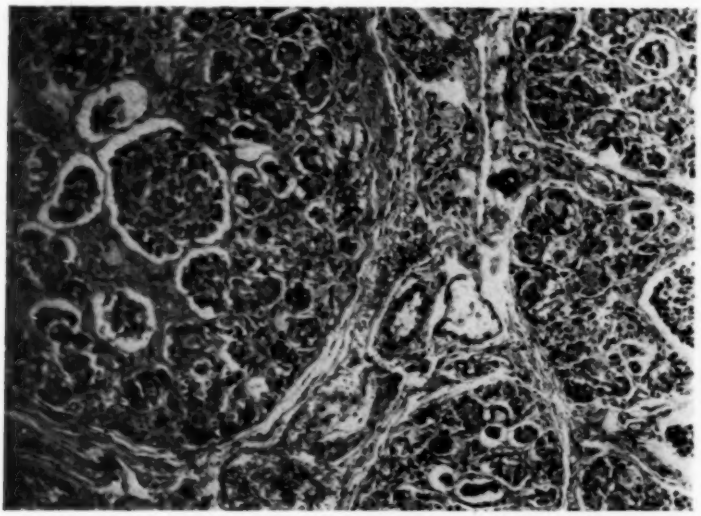

Fig. 4 (Case 4).—Pancreas: typical diffuse interstitial fibrosis, poor acinar development, prominent islands of Langerhans and cystic dilatation of ducts.

there was an accompanying mixed inflammatory cellular exudate in which mononuclear cells predominated although there was a fair number of polymorphonuclear cells. The acute process was characterized by a frankly suppurative exudate which irregularly filled many of the bronchi and bronchioles (Fig. 3). The pancreas showed changes characteristic of cystic fibrotic degeneration (Fig. 4).

Diagnosis.—The pneumonia in this case was quite extensive but the underlying process was one of an acute suppurative bronchiolitis.

Comment

The regularity with which persistent respiratory infections are associated with fibrotic degeneration of the pancreas is now generally appreciated. While it has been stated that the initial disturbance in the lung is one of mucosal metaplasia (due to vitamin A deficiency) with

secondary bronchiolitic and peribronchiolitic inflammation, typical mucosal changes are not always demonstrable. Furthermore, the respiratory infections characteristically occur within the first few weeks of life, at a time when it might be questioned whether the vitamin A deficiency changes could have developed sufficiently to be the initial factor. Such a statement does not, of course, imply that the nutritional deficiency does not play a significant part in the persistence of the respiratory disturbance nor that mucosal metaplasia is not one of the manifestations. Characteristically, the respiratory involvement is a bronchiolitic one although other secondary features such as suppuration and widespread pneumonia are commonly found at post-mortem examination.

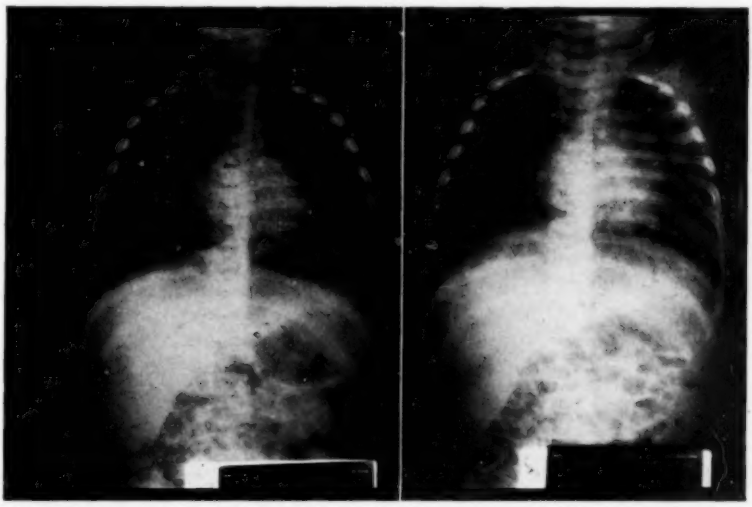

Fig. 5 (Case 5).—Roentgenogram of chest. Dorsal projections of thorax in inspiratory (left) and expiratory (right) phases of respiration. Notice the relative failure of the lungs to empty in the expiratory phase. The left lung is less obstructed than the right (empties to a greater degree in the expiratory phase). This difference between the two lungs is not apparent from a study of the diaphragm, which moves very little during respiration; it is evident, however, in the upper portions of the left lung space.

ACUTE BRONCHIOLITIS

(Acute Interstitial Pneumonia, Pneumonitis, Capillary Bronchitis)

CASE 5.—W. J., Negro male infant, 5 months of age, was admitted to the hospital Jan. 15, 1943, and died Jan. 19, 1943. There was a history of "cold" for ten days with wheezing type of respirations for five days. At the time of the hospital admission, there was marked dyspnea, with rapid grunting type of respirations and some retraction of the lower border of the chest. Crepitant râles were scattered throughout the chest, and the expiratory phase was roughened and prolonged. Fluoroscopic and roentgenographic examinations revealed a bilateral diffuse bronchopneumonia with marked obstructive emphysema (Fig. 5). The diaphragm was depressed and its excursion limited. Throat culture disclosed no unusual bacteria and the blood culture was negative.

The temperature ranged between 102 and 104° F. throughout the hospital period, and was unaffected by continuous sulfonamide administration. Other treatment consisted of administration of oxygen with intermittent carbon dioxide and oxygen and humidification of the air. No relief was obtained from aminophylline. Bronchoscopic aspiration was not employed because of the absence of any evidence of moisture in the larger air passages. While the infant appeared desperately ill, the outstanding feature was the dyspnea and not the toxicity. Exhaustion was an important factor in the cause of death.

Impression.—The impression was acute bronchiolitis.

Pathologic Report

Gross Findings.—(The right lung weighed 75 Gm. and the left, 65 Gm.) The lower lobe of the right lung was devoid of crepitation and contained nodular areas which were resistent to palpation. The cut surface revealed numerous small greyish red elevations. The lower lobe of the left lung was also congested and gave the impression of decreased crepitation. However, on cut section there were fewer areas of consolidation than in the right lower lobe. The upper lobes contained irregular patches of atelectasis which were dark red in color and were depressed below the surrounding surface which was pale and crepitant.

Microscopic Findings.—The microscopic pathology of the lung represented a very extensive bronchiolitis involving the very finest ramifications of the bronchioles. In the smaller bronchioles the lumina were completely filled with a purulent exudate. The inflammatory process had progressed in many of these bronchioles to the point where the entire mucosa had been destroyed and beginning bronchiolar abscesses were developing (Fig. 6). Much of the exudate was composed of broken down cellular debris. There were occasional colonies of bacteria, apparently staphylococci. The inflammatory reaction was not restricted to the finer divisions but involved the entire tracheobronchial tree as well.

The entire process was irregularly distributed; there were some areas where secondary lobular pneumonia had occurred; in other places the inflammatory reaction had extended from around the bronchi to the regional lung alveoli as a bronchopneumonia. Areas of atelectasis and of compensatory emphysema were also noted throughout both lungs, the atelectasis in many instances being obviously associated with plugging of the bronchi. There were terminal edema and marked congestion. In some of the larger bronchi the exudate had been present for a sufficient period that it had undergone hyalinization much as a thrombus does and in one or two places beginning organization of this exudate could be made out.

Diagnosis.—The diagnosis was acute tracheobronchitis; acute suppurative bronchiolitis; lobular and bronchopneumonia; atelectasis and compensatory emphysema; terminal edema and congestion.

CASE 6.—J. E., Negro male infant, 6 months of age, was admitted to the hospital Jan. 23, 1943, and dismissed April 4, 1943. The onset began with fever and a dry cough five days before hospital admission. There was increasing respiratory distress which was marked at the time of admission. Percussion was impaired over the right lower chest posteriorly. Elsewhere the chest was resonant to hyperresonant. Expiration was roughened and prolonged and there were crepitant râles

scattered throughout the chest. Fluoroscopic and roentgenographic examinations revealed bilateral patchy pneumonia, consolidation in the right lower lung (considered to be atelectasis) and a marked degree of obstructive emphysema. Initially the throat culture contained no unusual bacteria but during the fourth week, Type VI pneumococci were isolated. The infant was extremely ill for the first two weeks. The temperature ranged from 104 to 106° F. and was unaffected by sulfonamide medication. During this time, oxygen was administered continuously. The convalescence was prolonged and there were several exacerbations characterized by increased respiratory distress. During the last two to three weeks of the hospital period there was definite

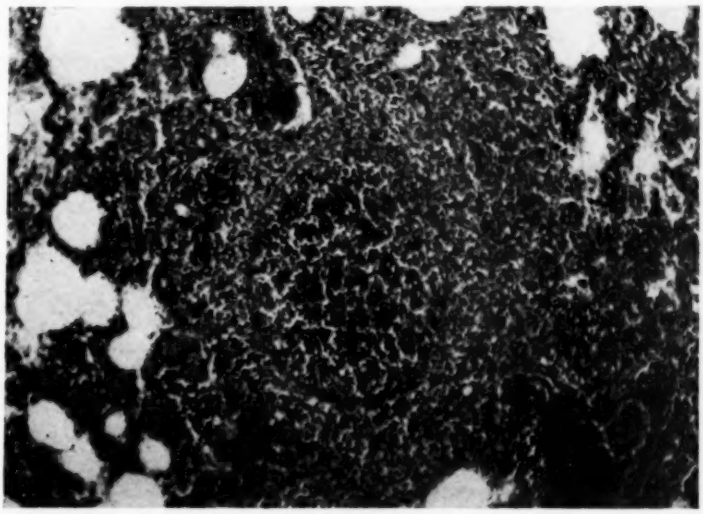

Fig. 6 (Case 5).—Section of bronchiole which can be identified only by indefinite persistence of wall. Lumen is full of suppurative exudate. There is destruction of mucosa and beginning bronchiolar abscess formation. Secondary pneumonia can be seen.

improvement although some evidence of obstructive emphysema and the atelectasis in the right lower lobe persisted in spite of bronchoscopic aspiration.

Impression.—The impression was of acute bronchiolitic infection, probably viral in origin, with secondary infection; persistent atelectasis of right lower lobe, and diffuse chronic bronchiolitic and interstitial changes.

CASE 7.—T. G., white male infant, 4 months of age, was admitted to the hospital March 29, 1944, and dismissed April 12, 1944. There was a history of "cold" of increasing severity with the onset four days prior to admission. Dyspnea was noted for the first time on the morning of admission. At this time, the infant appeared acutely ill. There were cyanosis and rapid respirations with moderate inspiratory retractions. The percussion note was hyperresonant; expiration was prolonged and roughened. There were no râles but occasional rhonchi. Fluoroscopically and roentgenographically, there was marked evidence of obstructive emphysema. Bronchoscopic examination showed only

mild congestion of the larynx, and aspiration of the trachea and bronchi resulted in only a small amount of a rather thick secretion. The throat culture contained a few Type IV pneumococci, which were not present in the culture of the bronchial secretion. The temperature was never markedly elevated, the peak being 100.8° F. In spite of this, the infant was in a serious condition for the first week or so in the hospital. The symptoms of respiratory obstruction were much more marked than were those of toxicity. At the time of dismissal, while the infant was greatly improved, there was still some prolongation of expiration as evidence that there had not been complete resolution of the bronchiolitic process.

Impression.—The impression was acute bronchiolitis.

Comment

These cases are presented as examples of acute infectious bronchiolitis (acute interstitial pneumonia). While the etiology is not known, they differ from other infections of the respiratory tract in their failure to respond to sulfonamide medication. The outstanding clinical feature is the marked dyspnea which, while it may be lessened somewhat by the administration of oxygen, is not completely relieved by it, nor is it affected by epinephrine or aminophylline. It may be of some significance that these cases appear to be more prevalent during periods when so-called primary atypical pneumonia (virus) is present among older children and adults. Severity of infection varies tremendously. In a great many instances, the infant shows only moderate dyspnea, and the course is self-limited without need of oxygen, humidification, or other treatment. The most severe form of the infection is represented by Case 5. Between these two extremes, there are all degrees of severity.

ACUTE TRACHEOBRONCHITIS

CASE 8.—D. Z., female infant, 9 months of age, was admitted April 12, 1943, and died April 13, 1943. There was a history of respiratory infection for forty-eight hours with increasing dyspnea for the latter twenty-four hours. There was an allergic history including skin eruptions and asthma since 3 months of age. There was no evidence of laryngeal obstruction. There was slight retraction of the lower portion of the chest with inspiration. The chest was resonant to hyperresonant and fine râles were heard over most of the chest. No rhonchi were heard. Fluoroscopically, it was observed that the excursions of the diaphragm were restricted and there was bilateral obstructive emphysema. The clinical diagnosis was acute bronchiolitis, and it was decided that bronchial aspiration was not indicated. The temperature at admission was 102° F. and during the next twelve hours rose to 107° F. at which time the patient died.

Impression.—The impression was acute bronchiolitis.

Pathologic Report

Gross Findings.—The tongue, larynx, trachea, bronchi, and lungs were removed as a single unit. There was no edema or obstruction of the larynx. The distal one-third of the trachea and both bronchi as

far as they could be dissected were filled with a thick, greenish grey, mucinous, tenacious exudate. While it did not actually form a cast of the respiratory tree, when it was grasped with forceps it could be pulled out as long stringy masses.

(The left lung weighed 45 Gm., and the right, 55 Gm.) The lungs were moderately emphysematous except along the posterior borders and medical surfaces where there were several small areas of atelectasis. These measured from a few millimeters to about a centimeter in diameter. They were neither sufficient in number nor congested enough to be typical of those seen in viral pneumonia. The lungs floated in water and when sectioned showed no gross evidence of consolidation, hemorrhage, or bronchiolitis. The pathology appeared to be limited to the distal trachea and the bronchi, with the parenchyma of the lung appearing to be in a fairly healthy condition. The pleural cavities were normal.

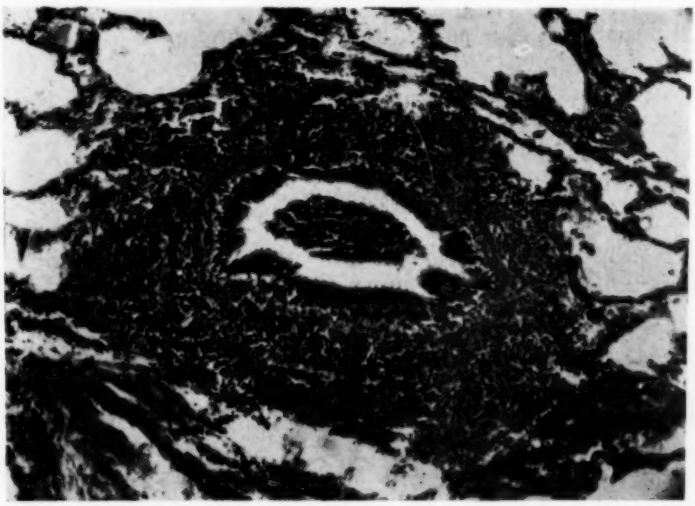

Fig. 7 (Case 8).—Section reveals peribronchiolar thickening of relative long duration as noted in the text, as well as the terminal acute suppurative bronchiolitis characterized by intraluminal purulent exudate.

Microscopic Findings.—The microscopic changes suggested an inflammatory type of reaction of several weeks' duration involving the medium-sized and larger bronchi. This was characterized by marked thickening of the peribronchial tissues which were infiltrated by chronic inflammatory cells, with plasma cells, lymphocytes and large mononuclears predominating. There were a generous distribution of eosinophiles and some increase in the fibrous tissue. This resulted in plication and thickening of the lining mucosa. Such a reaction suggested some type of chronic allergic inflammation. In addition, there was a terminal superimposed acute suppurative process (Fig. 7). This affected principally the smaller bronchioles and extended out into the terminal alveoli as a patchy lobular pneumonia. There were spotty atelectasis and compensatory emphysema. In one or two areas there were beginning metaplastic changes of the lining bronchial mucosa with a loss of ciliated epithelium and a tendency toward squamous transition. This was not marked nor complete but was quite definite.

Diagnosis.—The diagnosis was acute and chronic tracheobronchitis; acute terminal bronchiolitis; lobular pneumonia.

Comment

This case illustrates the probability that there may be no sharp demarcation between the clinical condition which is termed acute laryngotracheobronchitis and that under discussion in this communication as acute bronchiolitis. Elements of both were present in the lungs of the infant although clinically the manifestations were those considered to be characteristic of bronchiolitis. Of more than passing moment was the clinical decision that bronchoscopic aspiration was not indicated. We have been inclined to recommend intratracheal or bronchoscopic aspiration when there is evidence of moisture in the larger air passages. There was no such evidence in this infant. In spite of this, the gross observation at autopsy pointed to a greater involvement in the distal trachea and in the bronchi than in the more distal portions of the bronchial tree. It is evidence such as this which makes one less certain of his ability to determine which cases would be benefited by tracheal and bronchial aspiration.

ASPIRATION OF ZINC STEARATE

CASE 9.—M. S., a white female infant, 6 months of age, who had been in excellent health, was given a can of zinc stearate to hold while the mother prepared her crib. Almost immediately after the mother's back was turned, the baby coughed and it was found that the baby's face and neck were covered with powder. The infant immediately became dyspneic. Attempts were made to remove the powder from her mouth, but there was no relief from the dyspnea, and she was brought to the hospital about eight hours after this incident. The infant was extremely restless, anxious, and there was marked dyspnea with moderate cyanosis. The chest was resonant. The roentgenograms showed evidence of marked bilateral emphysema. The cyanosis was relieved for a time by oxygen, but respirations became more labored. Cyanosis reappeared in spite of oxygen in helium and the child died about twenty-four hours following the inhalation of the powder.

Pathologic Report

Gross Findings.—The lungs were markedly emphysematous, almost completely covering the anterior pericardial surface. There were numerous flakes of an amorphous white material lodged in the pyriform sinuses around the epiglottis, in the ventricles of the larynx, and sticking to the walls of the trachea and bronchi. There was no obstruction of the larynx, trachea, bronchi nor of their finer divisions as far as they could be dissected. Along the posterior borders of both lungs there were numerous small, but well demarcated, depressed areas of atelectasis. There was no other evidence of consolidation. When the lungs were sectioned, numerous lobules of lung tissue were outlined by white borders against the normal pink background. Where bronchioles ran parallel to and just below the surface they could be traced as white lines. When such areas were milked, material resembling tooth paste was squeezed from the cut ends.

Microscopic Findings.—The finer bronchioles were obstructed by detritus consisting of cells of an acute inflammatory reaction and an amorphous material (Fig. 8). The walls of the bronchioles were infiltrated by polymorphonuclear neutrophiles. The walls of the alveoli were thickened by congestion and there was some evidence of a very early inflammatory process suggesting an interstitial pneumonitis.

Comment

The embarrassment to respiration was probably the result of two factors: a mechanical obstruction and an inflammatory process caused by the irritation of the zinc stearate. Clinically, the features were those of an acute bronchiolitis with marked obstructive emphysema.

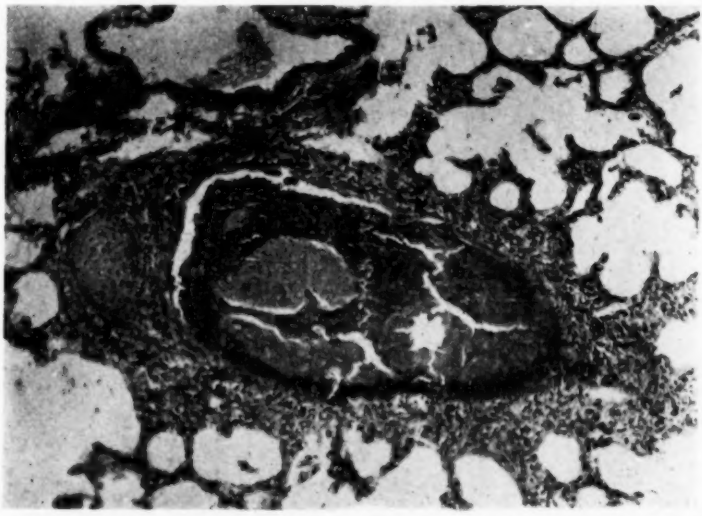

Fig. 8 (Case 9).—Section through a small bronchus, the lumen of which is filled with an acute inflammatory exudate admixed with zinc stearate. Note destruction of the mucosa and the adjacent emphysematous changes.

CHRONIC PASSIVE CONGESTION

Case 10.—M. D., white male infant, 5 months of age, was admitted Jan. 30, 1944, and died Feb. 11, 1944. This infant was a Mongolian idiot who had had respiratory difficulty since birth. He was born of a difficult breech delivery, and it was thought that he had probably aspirated amniotic fluid during delivery. There were frequent cyanotic attacks during the newborn period and a history of frequent respiratory infections with a failure to gain weight prior to his admission to the hospital. At the time of admission, there was dyspnea characterized by rapid respirations and a moderate indrawing of the lower costal cage. On occasion the lips appeared slightly cyanotic during coughing attacks, but cyanosis was not otherwise observed. The chest was hyperresonant and expiration was prolonged and roughened. There were no râles but rhonchi were present. Fluoroscopically, the leaves of the diaphragm were seen to be depressed and the excursions were limited. Broncho-

scopically, a small amount of secretion was aspirated from the trachea and a diagnosis of tracheobronchitis was made. Clinically, a chronic interstitial pneumonia resulting from the aspiration of amniotic fluid at birth and subsequent infection seemed the more probable explanation. After eleven days in the hospital, during which time the clinical condition was essentially unchanged, there was a rise in temperature and the baby died suddenly the next day.

Pathologic Report

Gross Findings.—The larynx, trachea, and bronchi appeared normal except that they were filled with a frothy pale exudate. Considerable quantities of this material exuded when pressure was made on the lungs. The lungs were exceedingly heavy. The right lung weighed 93 Gm.; and the left, 62 Gm. There was a far-advanced, chronic passive congestion in the posterior portion of each lung where the tissue was solid

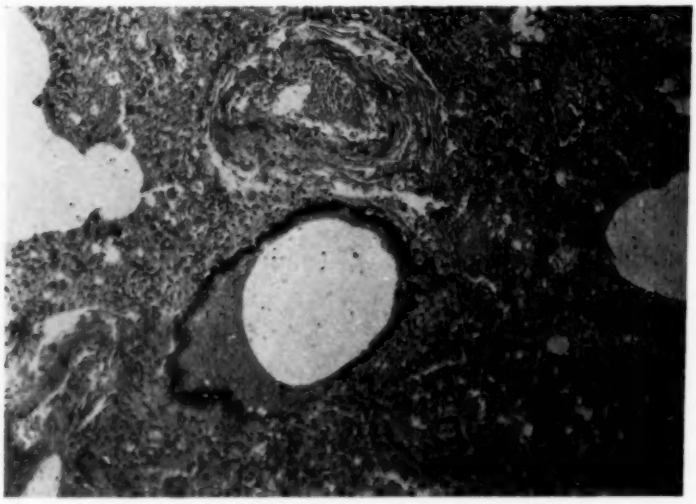

Fig. 9 (Case 10).—Field selected to show the edema and red cells within the bronchiolar lumen as well as the marked arteriolar sclerosis. Capillaries of the alveolar wall are distended and both serum and red cells are visible in alveoli.

and dark blue in color. When sectioned, there was no evidence of aeration. The anterior borders of both lungs were moderately emphysematous. The pleural cavities were normal.

The heart weighed 39 Gm., an approximate increase of 35 per cent over the average cardiac weight for infants at 5 months of age. There was no interatrial septum. The wall of the right atrium was hypertrophied and that of the left atrium was diminished in size.

Microscopic Findings.—The microscopic sections presented a very interesting and unusual picture. The entire pathology appeared to be related to the circulatory apparatus. There was an extreme degree of capillary congestion with the dilated capillaries standing out like grapes in the alveolar spaces. In many places this had resulted in the passive escape of red cells into the alveoli to a degree which might almost be termed hemorrhage. A certain amount of desquamation of the lining

cells and infiltration by large mononuclear phagocytic cells was observed but there was no evidence of any significant infectious inflammatory reaction. The hemorrhage in some places had become so marked that some of the smaller bronchioles were filled by it. Associated with this picture was a very remarkable degree of arteriolar sclerosis of the pulmonary arterioles and smaller arteries. This sclerosis was very similar to that seen in essential hypertension but was restricted largely to the pulmonary arterial circulation and was apparently a compensatory mechanism to maintain intrapulmonary blood pressure.

Diagnosis.—The diagnosis was congenital heart disease (absence of interatrial septum) with pulmonary congestion, hemorrhage, and associated pulmonary arteriolar sclerosis.

Comment

The autopsy findings were quite unexpected and placed an entirely different aspect on this case. The difficulty here was primarily a mechanical one resulting from the marked congestion of the pulmonary blood vessels and to a less extent from the blocking of alveoli and bronchioles by accumulation of blood in them. While this case is quite unusual, it illustrates another cause of generalized obstructive emphysema.

DISCUSSION

The foregoing cases are presented to illustrate the variety of conditions in infancy in which diffuse bilateral obstructive emphysema has been observed. It is not inferred that there are not other causes, as, for example, asthma, but at the moment there do not appear to be other common ones. In all of the described instances, obstructive processes in the smaller bronchioles were an important factor and in certain of them, notably, aspiration of amniotic fluid, acute infectious bronchiolitis, and aspiration of zinc stearate, bronchiolitic obstruction was the primary and most significant lesion. In these instances the original obstruction is most probably the expansile check-valve type as described by Jackson and Jackson,[1] and results from mucosal irritation and inflammation which produce edema and exudation. In the instances in which there is aspiration of a foreign material, the obstruction produced by it is an added factor. Peribronchiolitic or interstitial changes are a secondary but important and more or less constant accompaniment.

The expansile check-valve type of obstruction may assume several different forms, all of which presumably may be present at some stage of the disease or even at the same time in different parts of the lung. In general it is postulated that there is a sequential pattern with the initial obstruction being of the "by-pass valve" type in which air passes both in and out producing a "wheeze." This is followed by the "check-valve" type of obstruction in which air is admitted to the lung but very little is able to escape and obstructive emphysema of a marked degree is produced. When the obstruction becomes complete ("stop-valve"),

the trapped air is absorbed and the involved pulmonary tissue becomes atelectatic. In other instances, as for example, in chronic passive congestion of congenital cardiac disease and in miliary tuberculosis, the obstruction of the bronchioles is chiefly from without and is situated in the interstitial tissues.

While bronchiolitic lesions occur at all ages, the degree of respiratory embarrassment appears to be much greater in infants than in older children and in adults. It is probable that several factors may be responsible for this difference. These would appear to be the relatively thinner and less rigid thoracic cage, the relatively larger amount of interstitial tissue in relation to the bronchiolar and alveolar spaces, and the weaker musculature, but, particularly, the relatively small lumen of the bronchioles. At any rate, it is significant that severe bronchiolitic disturbances, except for asthma, are to a considerable extent, in the pediatric years, a problem of infancy.

In the differential diagnosis of the various conditions which may be responsible for obstructive emphysema, the age at onset of symptoms is helpful in certain instances. Aspiration of amniotic fluid must of necessity occur during birth and the symptoms should be evident during the first few days of life. The respiratory symptoms associated with cystic fibrosis of the pancreas, characteristically make their appearance within the first few weeks of life. Acute infections may and do occur during the newborn period but the opportunity for contact increases after the infant is removed from the hospital nursery.

Aspiration of amniotic fluid and its contents into the lungs may be assumed to occur in every newborn infant. Under ordinary circumstances the amount is small and the respiratory embarrassment insignificant. When large quantities are aspirated, however, obstruction of the respiratory tract results. Farber and Sweet[2] have described the pathologic appearance of the lungs under such circumstances and Wilson and Farber[3] have demonstrated that such aspiration is one of the causes of secondary atelectasis in the newborn infant. In those infants who die soon after birth, obstruction with atelectasis may be the principal pathologic change, but if the infant lives, even for relatively short periods (Case 1), there is distention of the alveoli in the aerated portions of the lung. Maegregor[4] has stated that congestion and edema are characteristically observed in the lungs of infants with aspiration pneumonia. While our interpretation of Cases 2 and 3 is inferential and speculative, it does not appear unlikely that a number of infants aspirate amniotic fluid and its contents in sufficient quantity to cause severe respiratory embarrassment without causing death. If this inference should be correct then it seems obvious that the prognosis must depend upon the extent of the respiratory changes, the capacity of the infant to compensate for them during the ensuing months, and upon the avoidance of respiratory infection. Immediate treatment should naturally consist of removal of the aspirated material but this is not

completely possible since by the time the baby is accessible, the aspirated contents have been drawn into the finer divisions of the lungs. Nevertheless, bronchoscopic aspiration may be helpful in clearing the trachea and larger bronchi. If there is secondary exudation, repeated aspiration might be beneficial. In some cases intratracheal aspiration by a catheter passed through a laryngoscope may be preferable. Since the principal difficulty is in the smaller bronchioles and alveoli, extreme care must be taken to avoid any trauma in the larynx. Oxygen is needed in practically all instances and carbon dioxide may be added for ten to twenty minutes of each hour to counteract the drying effect of oxygen.[5] Respiratory stimulants are not needed early and are not likely to be effective in the later stages of exhaustion. Ratcliff[6] has attributed improvement in two cases to the parenteral administration of human blood serum. He speculates that the intravascular osmotic pressure is increased so that it is effective in reducing the edema of the pulmonary tissues. The serum was injected intramuscularly and intraperitoneally in amounts of from 8 to 30 c.c. It is obvious that more evidence must be available before an effective relationship can be assumed. Therapeutic trials might also be made with intravascular injections of larger amounts of blood serum, of serum albumin, or of concentrated lyophilized plasma.

The consistent association of widely distributed respiratory infection with cystic fibrosis of the pancreas is now generally recognized.[7] However, we are not aware that attention has been called to the frequency with which obstructive emphysema is a feature of this respiratory involvement. The pulmonary changes are usually extensive but the bronchiolar and interstitial involvement appear to be fairly regular and important. To what extent the pulmonary involvement could be avoided by the early administration of vitamin A is not known but as stated previously, the changes in the case described here were not those usually ascribed to vitamin A deficiency. Furthermore, one cannot help being impressed by the frequency with which respiratory symptoms begin in the first few weeks of life and persist. It would seem doubtful that vitamin A deficiency would exert its effect in such a brief time. We do not, however, have any other explanation for the marked susceptibility to respiratory infections nor for the fact that they are persistent and usually the cause of death. We have been impressed by another case of cystic disease of the pancreas, not included in this series, who at the time of the initial examination (at 7 months of age) had a history of respiratory embarrassment dating back to the first week or two of life but who had evidence only of obstructive emphysema without signs of infection. Subsequently, the infant died of a respiratory infection which anatomically was shown to be a widespread suppurative bronchiolitic and pneumonitic infection. The interesting feature, however, was the period during which there was evidence of bronchiolitic obstruction with an expiratory type of dyspnea without

other clinical evidences of infection. In all infants who have a persistent diffuse respiratory infection or an expiratory type of dyspnea, cystic fibrosis of the pancreas should be considered in the differential diagnosis. In fact it is usually the respiratory disturbance which is responsible for the infant being brought to the physician.

While acute and even chronic bronchiolitic (interstitial pneumonia) infections are observed in infants following measles and pertussis, in our experience most of the instances of acute bronchiolitis appear to be primary. True, there is most often a history of a short preliminary period of several days during which the infant is thought to have only an acute upper respiratory infection, but there is usually no interval of remission of symptoms prior to the more or less abrupt onset of the dyspnea. There has been speculation that such acute infections may represent the infantile patterns of influenzal (viral) pneumonitis[8] and of primary atypical pneumonia. While the etiology was not established in the series of cases studied by Adams[9] the infection was thought to be a viral one. At the present moment, there appear to be a number of different viruses and possibly even certain bacteria which may be responsible for so-called primary atypical pneumonia. There is a tendency to segregate influenzal (viral) pneumonitis from this category. Marked destruction of the bronchiolar epithelium and interstitial inflammatory changes are considered to be characteristic of the influenzal infections and the obstructive dyspnea is adequately explained. The mortality among adults with primary atypical pneumonia is quite low, and less is known about its pathology but at least in one instance the changes observed were primarily those of a bronchiolitis.[10] Clinically, the majority of infants with acute bronchiolitis have in common an expiratory type of dyspnea, which is out of proportion to the evidences of toxicity, and a lack of favorable response to the sulfonamides. Determination of cold agglutinin titers as well as neutralization tests for specific viruses is definitely in order in infants who clinically have acute bronchiolitis in the hope that some information in regard to the etiology may be obtained.

While acute laryngotracheobronchitis as described by Jackson and Jackson[11], Sinclair[12], and others appears to be a different entity from that of acute bronchiolitis, it would appear from our case cited that there are instances in which there is no sharp distinction between them. Certainly, bronchiolitic involvement at least as a secondary phase is to be expected in acute laryngotracheobronchitis and conversely, when there is secondary infection of acute bronchiolitis, tracheobronchitis can scarcely be avoided. An important point in the individual case is the decision for or against bronchoscopic or intratracheal aspiration. Our own criteria are based on evidences of fluid or other obstruction in the larger air passages as indicated by a loose, productive cough or by rhonchi or coarse râles. It should be emphasized, however, that when the secretions become viscid, neither of these features may be present. For this reason, if the general condition of the child permits, a diagnostic

bronchoscopic examination is indicated provided facilities and skilled personnel are available.

Among the less frequent causes of obstructive dyspnea must be mentioned the aspiration of zinc stearate powder[13] and the case cited with chronic passive congestion secondary to a congenital cardiac lesion. It is possible that this type of dyspnea may also be produced by the pulmonary lesions of acute miliary tuberculosis. At least we have recently observed an infant in which this appeared to be a possibility.

A discussion of asthma is avoided, since it does not appear to be an important cause of obstructive emphysema during the first year of life.

SUMMARY

The clinical pattern of diffuse bilateral obstructive emphysema in infants has been described and cases illustrating a number of unrelated conditions which may be responsible for it are reviewed. These include aspiration of large amounts of amniotic fluid and its contents during or just prior to delivery, respiratory infections associated with cystic fibrosis of the pancreas, acute bronchiolitis (interstitial pneumonia), atypical forms of acute tracheobronchitis, aspiration of zinc stearate powder, and chronic passive congestion secondary to a congenital cardiac lesion.

While the pathologic lesions which are responsible for obstructive emphysema also occur in older children and adults, the clinical pattern and respiratory embarrassment are less pronounced than in infants.

It is speculated that the cases which have been termed acute bronchiolitis may in certain instances represent the infantile pattern of acute viral pneumonitis.

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HEALED ASYMPTOMATIC MILIARY TUBERCULOSIS

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THE recuperative power of the human organism over tubercle bacillus invasion has been much underrated in the past. Certain types of the infection in particular, such as infantile tuberculosis, tuberculous pneumonia, and miliary tuberculosis, have been lifted from the class of poor or hopeless prognosis to one of more favorable outlook.

The classification of miliary tuberculosis as an almost invariably fatal disease dates back to the pre-x-ray period of phthisiology when the disease was diagnosed by routine bedside examination in the acute pseudotyphoid or meningeal form or only on necropsy. The rare instances of retrogression of acute miliary tuberculosis with septic and toxic clinical syndromes could not change the generally malignant picture of the disease. The majority of case reports on chronic miliary tuberculosis belong either to the group of subsiding activity or of periods of apparent inactivity followed by reactivation. It is only more recently that subclinical and practically asymptomatic forms of evenly disseminated miliary tubercles throughout both lungs have been described.

Stivelman[1] described some exceedingly rare cases of healed or calcified miliary tuberculosis of the lungs without a history suggestive of preexisting pulmonary ailment. He stressed the point that no other pulmonary process gives quite the same roentgen appearance.

Liebermeister[2] classified miliary tuberculosis of the benign type in three groups: (1) cases having at first a benign course but later dying from the disease; (2) cases in which the miliary tuberculosis of the lungs disappears from the roentgen picture; and (3) cases in which miliary tuberculosis of the lungs persists, and is demonstrable.

Saye[4] detected miliary tuberculosis by routine x-ray examination in a number of healthy students.

Fish[3] reported ten cases of chronic miliary tuberculosis in children of which four recovered; however, all of them presented clinical symptoms of activity at one time or other.

Mayoral[5] described a case accidentally discovered with shotlike calcifications of uniform size and density within the lung fields, the individual being in excellent health and without any history of previous illness.

Beverly[6] reported five cases out of approximately 15,000 chest roentgenograms in which typical healed miliary tuberculosis was discovered.

From the Milwaukee Children's Hospital. Presented before the Ninth Annual Meeting of the American Academy of Tuberculosis Physicians in Chicago, June 13, 1944.

He stressed that the patients were not cognizant of the condition as there were no clinical signs or symptoms.

Geever[7] published in detail two case reports with x-rays, clinical and autopsy findings which showed miliary calcifications of the lungs, apparently due to completely healed miliary tuberculosis.

Cole[8] in a treatise on pneumoconiosis discussed the general question of chronic tuberculoid pneumoconiosis being responsible for some pictures of benign miliary tuberculosis.

The significance of the following case report lies in three facts: (1) the long observation for ten years prior to the evidence of miliary tuberculosis; (2) three years' observation following the diagnosis of miliary tuberculosis; (3) proof of practically uninterrupted, perfect health for two years prior and three years following diagnosis of miliary tuberculosis.

K. T., male infant, weight 7½ pounds, was born March 8, 1931. The family history was negative for tuberculosis. Development was normal during the first year.

The first admission to Milwaukee Children's Hospital was April 30, 1932, with the following diagnosis: broncho-pneumonia, peritonsillar abscess, thrush, and rickets. The treatment given was transfusion of 140 c.c. whole blood and incision of abscess. Two intradermal tests of 0.1 mg. old tuberculin were negative. Wassermann test was negative. The patient was discharged as recovered May 11, 1932.

The patient was not under observation for seven years. The history given by the mother and the school record (Table I) revealed that he was continually in good health except for uncomplicated measles in 1938 and occasional minor colds at various times.

The second admission was June 5, 1939. There was a history of slight head injury followed by fever, pains in the left ear, headache, and delirium. Evidence of acute tonsillitis, acute left otitis media, positive Kernig and Brudzinski signs. Spinal fluid: 2,900 leucocytes (90 per cent polynuclear), sugar 109 mg. Culture: *Streptococcus hemolyticus.* Treatment: neoprontosil and later sulfapyridine. He was discharged completely recovered June 30, 1939.

Re-examination at the outpatient department, July 11, 1939, revealed normal findings except for hypertrophic tonsils. An intradermal test with old tuberculin 0.01 mg. was positive one plus, repeated 0.1 mg. positive two plus. Sedimentation test 30 minutes, 2; 60 minutes, 8; 120 minutes, 20. An x-ray of the chest July 15, 1939, showed normal heart and mediastinum, area of questionable soft calcification in left hilar region, otherwise no evidence of tuberculosis or other pathology.

There were routine re-examinations on the following dates, Sept. 25, 1939, Oct. 13, 1939, Nov. 27, 1939, Sept. 23, 1940. In every instance the boy was symptom free and all physical findings were normal except for hypertrophic tonsils and slight cervical adenopathy. The school record revealed very few days of absence. On Nov. 27, 1939, blood count showed white blood cells 12,400; segmented, 37 per cent; stabs, 18 per cent; eosinophiles, 2 per cent; monocytes, 5 per cent; small lymphocytes, 33 per cent; large lymphocytes, 5 per cent.

On Oct. 20, 1941, the boy was called by the outpatient department for a routine annual re-examination on account of his positive tuberculin reaction. The following findings were obtained: His general condition

Fig. 1.

Fig. 2.

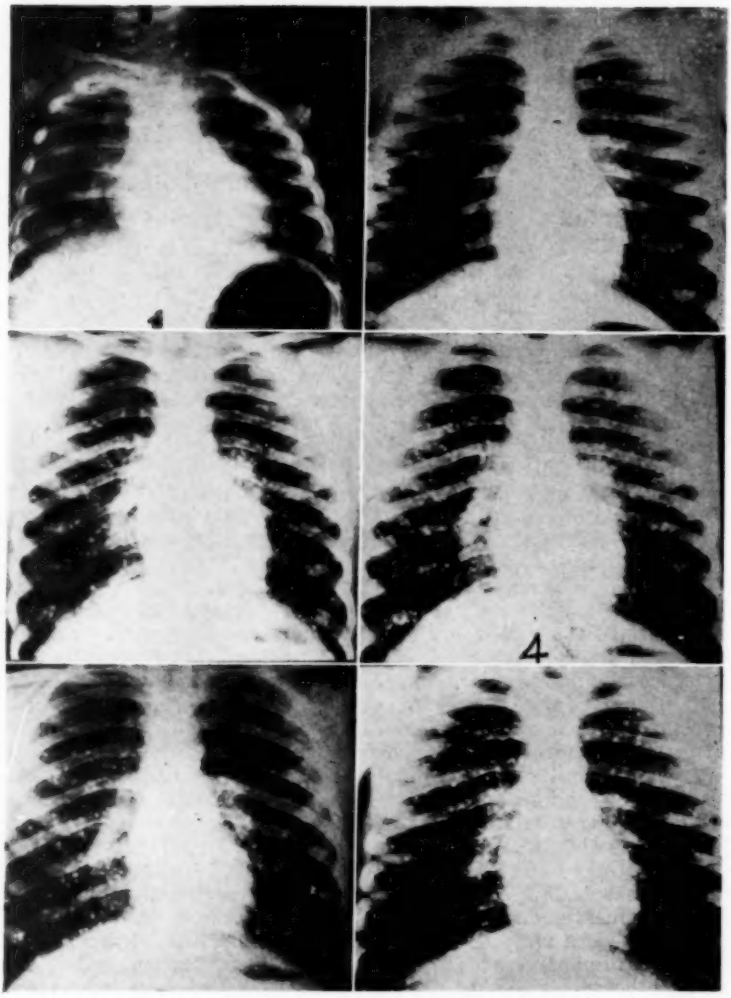

Fig. 3.

Fig. 4

Fig. 5.

Fig. 6

Fig. 1.—May 11, 1932, aged 14 months; bronchopneumonia; negative to 0.1 mg. old tuberculin.

Fig. 2.—July 15, 1939, aged 8 years, 4 months; recovered from streptococcus meningitis; positive to 0.01 mg. and 0.1 mg. old tuberculin; primary inactive hilum lesion with beginning calcifications.

Fig. 3.—Oct. 20, 1941, aged 10 years, 7 months; miliary nodular calcifications; gastric contents negative for tubercle bacilli; sedimentation rate, normal; continuously free from symptoms.

Fig. 4.—Aug. 24, 1942, aged 11 years, identical picture; persistent normal health; normal sedimentation rate.

Fig. 5.—June 7, 1943, aged 12 years, identical picture; normal health; normal sedimentation rate.

Fig. 6.—May 15, 1944, aged 13 years, identical picture; normal health; normal sedimentation rate.

was very good. He had no complaints, and stated that he had not been ill for the past two years. The physical chest findings were entirely negative; the cervical glands slightly enlarged. The x-ray picture showed evidence of bilateral tracheobronchial adenitis with marked calcification and a typical picture of evenly distributed miliary nodular calcifications throughout both lung fields. X-ray pictures of parenchymal organs (kidneys, spleen) were negative. On Oct. 20, 1941, the blood count showed white blood cells, 9,200; hemoglobin, 13 Gm.; segments, 40 per cent; stabs, 1 per cent; eosinophiles, 2 per cent; monocytes, 1 per cent; small lymphocytes, 52 per cent, large lymphocytes, 4 per cent; sedimentation rate, 30 minutes, 3; 60 minutes, 10; 120 minutes, 28.

On Nov. 3, 1941, stomach washings were inoculated into a guinea pig; on Dec. 15, 1941, autopsy was negative for tuberculosis. On Jan. 19, 1942, examination showed normal eyegrounds. On July 8, 1942, tonsillectomy and adenoidectomy were performed; histologic examination of tonsils was negative for tuberculosis. Re-examination was made by x-ray on the following dates: Aug. 24, 1942; Dec. 14, 1942; June 7, 1943; Nov. 29, 1943; May 15, 1944. Sedimentation rates after 30 minutes, 60 minutes, 120 minutes were as follows: Aug. 24, 1942, 3-10-25; Dec. 12, 1942, 1-4-13; May 15, 1944, 5-13-36.

At this writing he is a perfectly healthy-appearing 13-year-old boy; height, 59½ inches; weight, 91½ pounds; he is mentally alert, emotionally well balanced, and has an excellent school record. All x-ray pictures of lungs show invariably the identical findings of healed chronic nodular miliary tuberculosis.

TABLE I

RECORD OF SCHOOL ATTENDANCE

	DAYS ABSENT
Grade 1	
School year, 1937 to 1938	12
Grade 2	
School year, 1938 to 1939	22½
Grade 3	
School year, 1939 to 1940	16
Grade 4	
School year, 1940 to 1941	3
Grade 5	
School year, 1941 to 1942	2
Grade 6	
School year, 1942 to 1943	3

DISCUSSION

There is enough evidence in the literature to prove that hematogenous dissemination and possibly even lymphogenous or bronchogenic spread of tuberculosis may, in rare instances, occur practically free of clinical manifestations. There may be some who will question the possibility of asymptomatic tuberculosis in the active stage, especially authors like Wallgren who insist on the presence of clinical syndromes in every case of primary invasion, even if not recognized as such. The fact remains, however, that obviously healthy children, adolescents, or adults may be incidentally or accidentally (literally speaking) discovered as

bearers of pulmonary pathologic changes characteristic of miliary calcifications. The differential diagnosis between several etiological factors has to be considered: tuberculosis, tuberculoid pneumoconiosis, lymphosarcomatosis, coccidiosis, or other fungoid infections. In most cases, it will be an easy matter to rule out the more vicious nontuberculous diseases and to establish the diagnosis of benign, subclinical, healed chronic miliary tuberculosis. The two diagnostic factors are the roentgenogram and, as a rule, the positive tuberculin test. The bacteriologic findings are negative, the blood picture as well as the sedimentation rate are normal and there is no evidence of miliary tuberculous involvement of other organs. The value of this case report rests in the thoroughness of observation of a 13-year-old boy over a period of twelve years.

SUMMARY

1. An 8-year-old boy was found positive to tuberculin and he showed a roentgenogram of a healed primary tuberculosis with a normal hemogram and sedimentation rate.

2. Two years later, upon routine re-examination, with a perfect record of school attendance, he presented a roentgenogram of evenly distributed, healed, calcified miliary tuberculosis of the lungs. His general physical condition, hemogram, and sedimentation test were perfectly normal, and his stomach washings were negative for Koch bacilli on guinea pig inoculation.

3. Three years later the roentgenogram remained completely unchanged showing the identical evidence of miliary tuberculosis while his general health as well as all clinical tests remained entirely normal.

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INCIDENCE OF ENTEROZOIC PARASITISM IN CHILDREN

A Survey

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SURVEYS of enterozoic parasitism in children in the United States are few. Faust[4] made a survey of 1,100 cases, mostly children, in the New Orleans area in 1933. Kessel and Sinitsin[5] made a similar survey of 678 children in the Los Angeles area in 1938.

MATERIAL

The present survey was done exclusively on 512 children, medical patients of the Philadelphia General Hospital Pediatrics Department. The survey covered ten months with 658 surgical and 853 medical hospital admissions; most of the other 999 were hospitalized an inadequate time for enterozoic parasite study. The patients of this survey had the usual social and economic general hospital status.

METHODS

With complimentary cooperation of the hospital personnel and the Zoology Laboratory of the University of Pennsylvania the stools were transported to the examining laboratory within two to six hours following collection. Each stool was examined macroscopically for proglottids, adult worms, stool form, consistency, color, mucus, blood, and degree of digestion.

A routine Ringer's saline film was made to detect trophozoites in motion or locomotion. A Lugol's iodine wet film was also routinely studied. From this and the saline film, record was made of the extent of digestion of meat fibers, starch grains, etc.; presence of fatty acid crystals, Charcot-Leyden crystals, neutral oil; erythrocytes, leucocytes, and parasites, that is, adult worms, larvae, ova, trophozoites, precysts, and cysts.

Two iron-alum-hematoxylin stained films were made on each stool for cytological study and differential diagnosis. Either or both the de Rivas centrifugation and zinc sulfate centrifugal flotation method of concentration was or were done on each stool. No culturing nor perianal scrapings were included in this survey.†

This survey was made possible by the assistance of Dr. J. H. Clark of the Pathology Department of the Philadelphia General Hospital, and Dr. D. H. Wenrich of the Zoology Laboratory of the University of Pennsylvania. Dr. William P. Shields was essentially responsible for the clinical work-up and therapy.

*Now Captain, M.C., SAAAB.

†Culture usually requires specific media for the growth of the various protozoa parasites and considerable time for their identification, and too frequently adds little or nothing to the final total incidence. Perianal scrapings, which facilitate considerably *Enterobius vermicularis* ova diagnosis, could not be routinely done in the existing setup.

RESULTS

General Incidence.—Of 512 children examined 345, or 67.3 per cent, had enterozoic parasites. There was a total of 646 parasites, or 1.9 parasites per parasitized child (Table I). One child, aged 9 years, had five species, that is, *Taenia saginata, Trichuris trichiura, Endamoeba histolytica, Iodamoeba buetschlii,* and *Giardia lamblia.*

TABLE I

AGE GROUPS* (YR.)	PARASITES† (NO.)	PERSONS EXAMINED (NO.)	PARASITES PER PERSON
0 to 1	3	22	0.136
1 to 2	34	53	0.641
2 to 3	60	64	0.938
3 to 4	86	74	1.162
4 to 5	59	44	1.341
5 to 6	56	40	1.400
6 to 7	72	46	1.564
7 to 8	77	50	1.540
8 to 9	47	30	1.567
9 to 10	63	38	1.659
10 to 11	40	24	1.667
11 to 12	49	27	1.815
Totals	464	512	1.261 (1.3)

*Age group (yr.) is the chronological age of the patient.
†Parasites (No.) represents separate species.

Age Incidence.—The ages in the survey extended from 6 weeks to 12 years. The incidence of all parasites per person in age groups in years as shown in Table I indicated continual yearly increase.

A more complete analysis is presented in Table II. Here the age group from 2 weeks to 1 year contained *Endolimax nana* (a parasite of no clinical significance) in one infant 6 weeks old, and *Enterobius vermicularis* in an 8-month-old child. *E. histolytica* incidence remained fairly constant throughout the age groups. *Endamoeba coli* and *Endolimax nana* paralleled the same constant incidence rise throughout. *Iodamoeba buetschlii, Dientamoeba fragilis, Embadomas intestinalis* and *Trichomonas hominis* were too few to warrant comment other than that there was a suggestive incidence increase in later childhood years. *Giardia lamblia* rapidly increased and leveled off at 4 to 6 years of age where its incidence surpassed all others. The *Chilomastix mesnili* incidence made little response to increased chronological age of the host. *Ascaris lumbricoides, Trichuris trichiura* and *Taenia sp.* first appeared in the 3 to 7-year-old age groups.

Sex Incidence.—While the chronological ages were young in this survey there was definite suggestion that the incidence was higher in males (Table III). This corresponds well with the findings of Kessel and Sinitsin[5] and others.

DISCUSSION

This survey incidence of enterozoic parasitism in children approximated the generally accepted actual incidence, with few exceptions. In

TABLE II

PARASITE PER CENT*

AGE GROUPING (YR.)	RHIZOPODA					MASTIGOPHORA				NEMATODA			CESTODA		
	E. HISTOLYTICA	E. COLI	ENDOLIMAX NANA	IODAMOEBA BUETSCHLII	DIENTAMOEBA FRAGILIS	GIARDIA LAMBLIA	CHILOMASTIX MESNILI	RETORTOMONAS INTESTINALIS	TRICHOMONAS HOMINIS	ASCARIS LUMBRICOIDES	ENTEROBIUS VERMICULARIS	TRICHURIS TRICHIURA	TAENIA SAGINATA	TOTAL CASES IN AGE GROUP	TOTAL SPECIES†
0 to 1	00.0	0.00	9.1	0	0	0	0	0	0	0	4.5	0	0	22	3
1 to 2	7.5	24.5	18.9	0	0	15.1	0	0	0	0	0	0	0	53	34
2 to 3	6.2	23.4	26.4	0	4.7	26.4	0	6.2	0	0	0	0	0	64	60
3 to 4	13.5	21.6	31.1	4.1	4.1	33.8	0	2.7	0	0	4.1	0	0	74	86
4 to 5	9.1	27.2	34.1	0	2.3	45.4	9.1	0	0	0	4.5	0	4.5	44	59
5 to 6	7.5	40.0	27.5	5.0	5.0	40.0	5.0	2.5	0	0	0	0	7.5	40	56
6 to 7	8.7	52.1	37.0	0	6.5	39.1	8.7	4.3	4.3	0	4.3	0	0	46	72
7 to 8	8.0	52.0	40.0	0	6.0	30.0	10.0	0	2.0	4.0	10.0	0	0	50	77
8 to 9	10.0	56.7	26.6	0	0	40.0	16.7	0	0	0	6.7	0	0	30	47
9 to 10	5.3	50.0	44.7	2.6	5.3	39.5	7.9	5.3	5.3	2.6	7.9	2.6	0	38	63
10 to 11	8.2	69.7	57.4	0	4.1	41.7	4.1	0	4.1	0	4.1	4.1	4.1	24	40
11 to 12	11.1	51.8	44.4	3.7	7.4	37.0	7.4	3.7	3.7	3.7	7.4	0	0	27	49
Total	8.0	35.2	30.5	1.4	3.9	32.2	5.1	2.3	1.4	0.6	4.1	0.4	1.2	512	646

*Parasite per cent is the interpolated incidence of parasites per 100 children hosts based on actual survey incidence.
†Total species is the number of specific parasites per age group.

TABLE III

SEX INCIDENCE*

SEX	TOTAL EXAMINED	TOTAL NUMBER POSITIVE	TOTAL PER CENT POSITIVE	ENDAMOEBA HISTOLYTICA		ENDAMOEBA COLI		ENDOLIMAX NANA		IODAMOEBA BUETSCHLII		DIENTAMOEBA FRAGILIS		GIARDIA LAMBLIA		CHILOMASTIX MESNILI		RETORTOMANAS INTESTINALIS		TRICHOMONAS HOMINIS		ASCARIS LUMBRICOIDES		ENTEROBIUS VERMICULARIS		TRICHURIS TRICHIURA		TAENIA SAGINATA	
				NO.†	%‡	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO	%	NO.	%	NO	%	NO.	%	NO.	%	NO.	%
Male	245	176	71.8	22	9.0	94	38.3	82	33.4	4	1.6	9	3.7	88	35.9	13	5.3	6	2.4	3	1.3	1	0.5	12	4.9	2	0.8	3	1.2
Female	267	169	63.3	19	7.0	86	32.1	74	27.6	3	1.2	11	4.1	77	28.5	13	4.9	6	2.2	4	1.5	2	0.7	9	3.3	0	0	3	1.1
Total	512	345	67.3	41	8.0	180	35.2	156	30.5	7	1.4	20	3.9	165	32.2	26	5.1	12	2.3	7	1.4	3	0.6	21	4.1	2	0.4	6	1.2

*Sex incidence shows male children more frequently parasitized than females in these age groups with few specific exceptions.
†No. is the number of specific parasites.
‡% is per cent incidence.

the previously mentioned surveys essentially on children, Faust[4] (1933) found 6 per cent *E. histolytica* incidence in the ages from 1 to 5; and 15 per cent over 5 years of age at Charity and Welfare Clinics. Kessel and Sinitsin[5] (1938) found 3.3 per cent average in their Los Angeles survey. Our 8.0 per cent represented an intermediate incidence at another geographic extreme. Hegner and associates (1929) believed at least 50 per cent of the general population to be infected with *E. coli;* Kmeza (1939), at least 25 per cent. The incidence in this survey approximated these percentages. Craig (1934) believed that *Endolimax nana* had almost as high incidence as *E. coli;* our findings were in agreement. Faust[4] (1933) believed giardiasis to be a disease of children from 1 to 5 years old with a higher age incidence in that age group. This survey paralleled such incidence.* *Enterobius vermicularis* on the other hand was undoubtedly several times the 4.1 per cent incidence determined; however, fecal examinations seldom have given a higher incidence. Perianal scrapings, the best diagnostic procedure, probably would have made up the difference.

Repeated stool examinations were done on some few patients with the addition of about 8 per cent to their total incidence.

SUMMARY

1. The average incidence of enterozoic parasitism was 1.3 parasites per surveyed child. This incidence gradually increased from 0.14 parasites per child in the 0- to 1-year age group to 1.82 in the 11- to 12-year age group. A total of 67.3 per cent had enterozoic parasites.

2. Parasitized males (71.8 per cent) exceeded parasitized females (63.3 per cent).

3. An analytic incidence is presented; in some respects it exceeds other similar surveys but in general it parallels them.

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*The routine concentration techniques were largely responsible for the high protozoa incidence, particularly of *Giardia lamblia* and *Endamoeba coli* which both concentrate very well by the de Rivas centrifugation method.

EXANTHEM SUBITUM (ROSEOLA INFANTUM)

Report of Eighty Cases

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IN THE first three years of life infants and children are bedevilled by numerous cutaneous eruptions, the source of which is not always clear. Unless the eruption is one typical of the well-known exanthems (measles, German measles, scarlet fever, chicken pox) the connotations of teething rash, diaper rash, nettle rash, stomach and intestinal rash, prickly heat, and others are attached to it by the laity and even by many practitioners without curiosity as to the actual cause. It is with the thought of separating a well-known but not too well-recognized exanthem of infancy from the confusion of unclassified infantile rashes that this review is presented.

Exanthem subitum (roseola infantum, pseudorubella, exanthem criticum, rose rash of infants, sixth disease, etc.) is a self-limited, acute illness of infancy characterized by an initial fever of three to five days' duration and thereafter terminating in an erythematous, macular, or maculopapular eruption with predilection for the trunk, neck, and extremities. The disease is mildly contagious and is thereby considered infectious. In private practice cases occur singly or in small groups; in institutions epidemics of the disease have been reported. Recovery is the rule as soon as the eruption appears. The prognosis is always excellent, but harm may result from misdiagnosing and overtreating the illness and in grief to the parents by unnecessarily quarantining the home. Variations in the signs and symptoms of the illness occur frequently.

This malady is a definite clinical entity and is a disease entirely separate from any other eruptive fever of infancy and childhood. It was first described minutely by Zahorsky in 1910[1] and in 1913,[2] and again concurrently by Veeder and Hempelmann,[3] by Levy,[4] and Westcott[5] in 1921 before cognizance was given to its being a distinct disease, primarily confined to infants and young children, and to be included among the other acute infectious exanthems of childhood. There is no evidence that this is a new disease, but rather that it is a malady that has been confused with other exanthems for many decades. After the first report of the illness in America, physicians from many parts of the world reported similar cases in their practice. Many European investigators first believed that the illness was a manifestation of "grip" or influenza, or that the fever and eruption were the result of allergy, but subsequent reports from many countries were not in accord with those views. Since Zahorsky's first descriptions the nomenclature has become confused.

In a twenty-four-month period, May, 1942, through May, 1944, eighty children with roseola infantum from several rural communities were

examined. Most of the patients (seventy-two, or 90 per cent) were seen in the office; only a few (six, or 7.5 per cent) were followed entirely in the home. Two children (2.5 per cent) were observed in the hospital. White blood counts and differential counts were obtained on as many patients as possible, and these findings have been correlated with the phases of the disease (Figs. 5, *A* and *B*).

I. AGE OF PATIENTS

In our study it was found that roseola infantum occurred most frequently in infants of 6 to 18 months of age (Fig. 1). This finding is in general agreement with most writers on the subject. Our youngest patient was 5 months of age. One child 3 years of age and three children 5 years of age were also affected. Zahorsky[6] stated that only

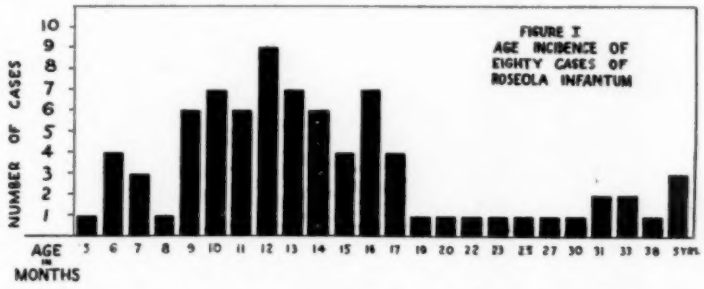

Fig. 1.—Age incidence of roseola infantum over two-year period from 1942 to 1944.

ten cases in children past the age of 4 years have thus far been recorded, so unusual is the disease in the older child. Cases have been reported occasionally in children up to the age of 14 years. Rare cases in adults have also occurred. Greenthal[7] observed a typical attack in an 18-year-old girl, and Cutts[8] described a typical case in an adult female aged 31 years.

The youngest case mentioned in the literature was in an infant 2 months of age.[6] Infants around the age of 12 months seem especially susceptible to the disease.

Practically all of the patients were healthy; all were well developed and well nourished. In fact, for many, roseola infantum was their first illness.

Formerly it was believed that only bottle-fed infants contracted the disease; later reports revealed that the illness may also occur in breast-fed infants. In our series one-fourth of the infants of 12 months or younger had nursed from four to twelve months at the breast.

II. SEX

Our cases were almost evenly divided between the sexes, forty-two male (52.5 per cent) as compared to thirty-eight (47.5 per cent) female patients (Fig. 2). There was a definite increase in male infant cases in the age period of 12 to 24 months. In Glanzmann's[9] series, males

outnumbered females by the ratio of 3:2. The sexes were about equally divided in the reports by Barenberg and Greenspan,[10] Rosenbusch,[11] Greenthal,[7] Breese,[12] Yoshina,[13] and Jennings.[14]

III. SEASONAL INCIDENCE AND EPIDEMIOLOGY

Forty-eight cases (55 per cent) in our study occurred during the months of February, March, and April (Fig. 3). As many cases (thirteen patients or 16 per cent) occurred in October as did in February and April. Infants with the illness were seen in every month of

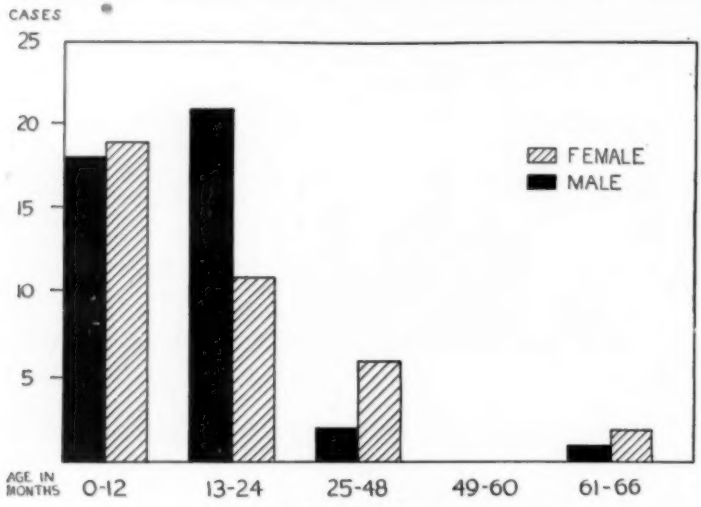

Fig. 2.—Sex incidence of roseola infantum.

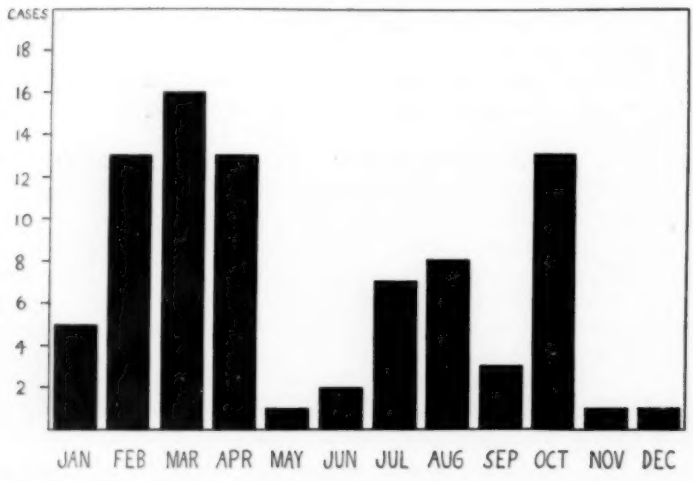

Fig. 3.—Monthly incidence of roseola infantum over two-year period from 1942 to 1944.

the year. Roseola infantum apparently has definite seasonal variation, tending to occur most frequently in the spring months with an increase in October. Relatively few cases were seen in the months of May, June, November, and December. Fig. 4 shows the monthly incidence of roseola infantum in this report from May, 1942, to May, 1944, compared with the number of cases of measles, German measles, and scarlet fever reported to the Yuba-Sutter County Health Department during the same period. It will be seen that an increase in the morbidity of roseola infantum almost coincides with an increase in incidence of the other acute exanthems. Many observers have remarked on the increase of roseola infantum during the months when coryza is prevalent.

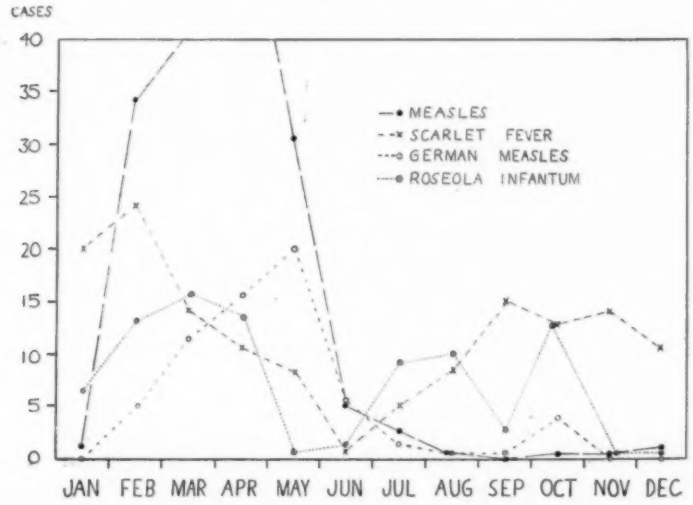

Fig. 4.—Morbidity of roseola infantum in this report compared with that of measles, scarlet fever, and German measles reported to the Sutter-Yuba Health Department for the two-year period from 1942 to 1944.

IV. ONSET (TABLE I)

In fifty-seven cases (71.2 per cent) the onset was sudden with mild or few prodromal symptoms. The onset began with fever usually at night in fifty-two of these patients. In the majority of the patients no prodromal symptoms occurred prior to the fever. Of twenty patients (25 per cent) the mothers believed the children to be having an upper respiratory infection but only to a mild degree. Most writers have discredited the importance of coryzal symptoms in the illness, but we believe them to be part of the symptom-complex of roseola infantum analogous to the upper respiratory symptoms in measles. Faber and Dickey[15] have stated that "a mild coryza is not infrequent. Occasionally a severer nasopharyngeal infection is present with mucopurulent discharge from the nose, edema of the pharynx and uvula, and slight exudate on the tonsils." The tendency for the temperature to rise to

heights of from 105 to 106° F.* occurred frequently. In five infants convulsions occurred when the fever was 105° F. and over. The cause of the convulsions was believed to be a result of cerebral irritability due to the fever rather than from the disease per se, because in no infant did the convulsion recur once the fever was controlled. Irritability and malaise were constant symptoms in almost all the cases.

TABLE I

TYPES OF ONSET OF ROSEOLA INFANTUM

	CASES		PER CENT
Sudden or abrupt	57		71.2
Fever and Restlessness	42	52.5	
Fever alone	10	12.5	
Vomiting	5	6.2	
Upper Respiratory Infection (Coryzal symptoms)	14		17.5
Diarrhea	4		5.0
Fever with Convulsion	3		3.7
Tonsillitis and Pharyngitis	2		2.5

V. COURSE OF THE ILLNESS (TABLES II AND III)

a. *Fever.*—Generally speaking, three days of fever transpired before the eruption occurred. In one case as far as the mother was able to ascertain by use of the rectal thermometer, there were only two days of fever preceding the rash. In seven cases the increase in temperature extended to five days and then the rash followed. In sixty-two cases the fever was of the intermittent type, the temperature varying from 102 to 106° F. for the first forty-eight hours and from 100 to 103° F. the next forty-eight hours. In the other eighteen cases the fever was definitely of the remittent type, the temperature declining to normal levels between rises. In the cases with the remittent type of fever irritability and fretfulness waned as the temperature fell, while in patients with the intermittent type of fever irritability and peevishness were constantly present day and night.

b. *Eruption.*—After the course of fever the eruption appeared in fifty-three cases (66 per cent). In thirty-five infants (43.7 per cent), however, the rash occurred fully twenty-four hours prior to the return of the temperature to normal. In two patients the temperature had been normal for twenty-four hours before the typical exanthem of roseola infantum made its appearance. Seventeen patients (21 per cent) were brought into the office after the rash had appeared and when the illness had run its course, mainly because their parents were told by friends that the infant had measles. The exanthem characteristic of the disease has been described for the most part as being macular. In our series maculopapular and papular rashes were constantly seen rather than only the macular type. The lesions were discrete in the early stages, and were often seen first on the lower abdomen, back, and neck. In eighteen cases early lesions were seen first behind the ears and on the neck as well as on the trunk. Few or no

*All temperature readings recorded in this report are rectal.

lesions occurred about the nose and lips. The face was spared of lesions in most of the cases, although in some of the patients a few scattered lesions of the cheeks as well as slight swelling and redness of the cheeks and eyelids were presnt. Over the body the lesions were discrete for the most part, but the eruption tended to become confluent in some of the cases. The exanthem seemed to fade in similar fashion to that of measles but much quicker. Slight pruritus of the fully blown exanthem was occasionally seen in the child past 12 months of age. Most writers deny the presence of pruritus, but Stafford[16] stated "the rash causes some discomfort from itching and stinging." In eight of the cases a fine faint branny desquamation was seen. Pigmentation was not present in any of the patients.

About forty-eight hours prior to the exanthem, an erythematous ananthem of specks and streaks on the soft palate was seen in seventy cases (87 per cent). This ananthem coincided with the height of the tubotympanitis and the faucial and pharyngeal congestion.

Within twenty-four to thirty-six hours after the cutaneous eruption appeared almost all the flushing of the tonsils, throat, and eardrums had faded.

c. *Duration of Illness.*—The period of illness varied from five to nine days with the average period at six days. Generally the convalescent stage extended to a period of forty-eight hours after the rash appeared. The demarcation between the acute and convalescent stages of roseola infantum was sharp and crisis-like in fifty-two of the pa-

TABLE II

PHYSICAL FINDINGS DURING COURSE OF ROSEOLA INFANTUM

		CASES		PER CENT
Fever		80		100.0
Eruption		80		100.0
Lymphadenopathy		78		97.5
Occipital Group	77		96.2	
Posterior Auricular Nodes	75		93.7	
Superficial Cervical Group	36		45.0	
Generalized	31		38.7	
Flushing of Eardrums		74		92.5
Constipation		32		40.0
Upper Respiratory Infection		20		25.0
Diarrhea		12		15.0
Desquamation		8		10.0
Meningismus		4		5.0

TABLE III

SYMPTOMS DURING COURSE OF ROSEOLA INFANTUM

	CASES	PER CENT
Irritability	74	92.5
Anorexia	64	80.0
Abdominal Pain	20	25.0
Cough	9	11.2
Headache	4	5.0
Earache	2	2.5
Aching Joints	2	2.5
Pruritis of Exanthem	1	1.2

tients. Irritability and malaise often extended throughout the entire illness especially when they were marked at the onset.

d. *Unusual Symptomatology.*—Occasionally the onset of the illness may be quite severe and be suggestive of meningitis or encephalitis. Wallfield[17] reported a case of roseola infantum in a male child 7 years of age, that had an encephalitic type of onset. Stafford[16] reported two cases of roseola infantum with neurological findings. In our series four infants had meningismus, and meningitis was considered a possibility for a time. No spinal punctures were performed, but in other such cases reported where the spinal fluid had been withdrawn, no abnormality had been noted.

Pain in the abdomen may be a disconcerting symptom especially when appendicitis must be excluded. Following is a brief summary of a case of roseola infantum in a 5½-year-old male whose chief complaint was abdominal pain.

D. W., always in good health except for an attack of measles in 1941, began to complain of abdominal pain on Oct. 20, 1943. The pain continued for the next two days and then he was seen in the office. Examination revealed an irritable, well-developed and well-nourished boy who complained of pain whenever pressure was made over the right lower quadrant. Definite resistance to pressure was present in that area. The temperature was 103° F.; pulse, 120 per minute; respirations, 26 per minute. The lungs were negative. The throat was moderately congested. The rectal examination was essentially negative. The white blood count was 7,000 per cubic millimeter with 66 per cent polymorphonuclear leucocytes and 34 per cent lymphocytes. Symptomatic treatment was instituted. On Oct. 24, 1943, the fever suddenly returned to normal and a rose-red maculopapular eruption typical of roseola infantum appeared. Recovery was complete two days later.

A mother, 25 years of age, who brought her 10-month-old daughter to the office with the eruption of roseola infantum and gave the usual antecedent history of the child's case, stated that her own neck began to hurt that morning. Examination of the mother revealed the presence of moderately enlarged and only slightly tender lymph nodes of the lateral cervical chains. The occipital nodes were enlarged also. The throat was slightly congested; the eardrums were normal. There was no complaint of malaise. The lymphadenopathy subsided two days later. A blood count was not obtainable. This mother possibly had modified roseola infantum, having contracted the illness from her infant daughter.

VI. INCUBATION PERIOD

Despite a careful history in each patient we were able to obtain only five records of contact with a case of roseola infantum. In three of these instances approximately thirty days transpired between the initial contact and the start of the fever. In two instances three days separated the contact and the onset, and in one case five days appeared to be the incubation period. We do not propose to suggest thereby that three to thirty days is the incubation period in the home for roseola infantum. Cushing,[18] in a hospital epidemic of the disease in Montreal found the incubation period to be ten days on the average.

Barenberg and Greenspan[10] had a similar experience in New York City and thereby confirmed the report of Cushing. Ryden[19] reported similar findings.

VII. LABORATORY FINDINGS

a. *Blood Counts.*—Forty-five white blood counts and differential counts were performed on thirty-six patients during the first five days of the illness and the findings have been tabulated (Fig. 5). Veeder and Hemplemann[3] in 1921 were the first to make use of the blood count as an aid in diagnosis of the disease. The leucopenia that is characteristic of the disease is most pronounced on the third day of fever. In one infant of 14 months, the white blood count was 8,000 on the second day, but this had fallen to 2,900 by the third day; on the fifth day the count had risen to 6,700. A progressive relative decrease of the polymorphonuclear cells and an increase in the lymphocytes occurred on the second, third, fourth, and fifth days and was most marked on the fifth day. It was noted also that as the lymphocytes increased in the peripheral differential count that the palpable lymph nodes increased in size and in many infants these were slightly tender to touch.

Fig. 5 reveals the fall of the white blood count during the period of fever before the exanthem appeared, reaching its lowest level on the third day of fever. When the rash appeared the leucopenia gave way to the normal white blood count. By doing white blood counts on the first and third, or second and third days of the illness, it may be possible in many instances to prognosticate the eruption and thus give the parents a favorable opinion as to the conclusion of the case. On the second, third, and fourth days of the illness band forms, varying from 4 to 18 per cent, were seen frequently in the differential counts. The monocytes were increased as high as 17 per cent in many instances. Many investigators have remarked on the absence or diminution of the eosinophiles. This we found to be true also in our cases. Such a consistent finding, however, is not in accord with the proposed allergic causology of the disease. Disrupted basket cells were often typically seen on the fourth and fifth days. No abnormalities of the erythrocytes were seen. Hemoglobin values showed little variation from the normal.

b. *Blood Cultures.*—Culture of the blood was undertaken in four cases, but no organisms were grown in any instance. The etiology of roseola infantum has been obscure since it was first mentioned in the literature, but many of its features point toward its being an infectious disease. Since the early descriptions of this illness little work has been done in determining its etiology. The theory that a virus is responsible for roseola infantum appears to be the consensus of opinion among many writers because the disease is in some respects analogous to measles and German measles. Breese[12] working with five infants in the pre-eruptive stage attempted to demonstrate a filtrable virus from the filtered throat swabbings of three infants through animal

inoculations but without success. He also cultured blood from one infant and the throat swabbings of another on chorioallantoic membrane of a chick embryo but no virus was demonstrated.

c. *Urinalysis.*—Examination of the urine in thirty-eight patients was essentially negative. In six cases a slight increase in pus cells over the normal and an occasional blood cell were noted. Slight transient albuminuria was detected in four cases during the height of the fever. Similar findings have been mentioned in the literature.

d. *Roentgenologic Examinations.*—Roentgenograms of the chest were taken on four subjects, but no abnormalities were noted such as the infiltration and increase in hilar bronchovascular markings often seen in cases of uncomplicated measles.[20]

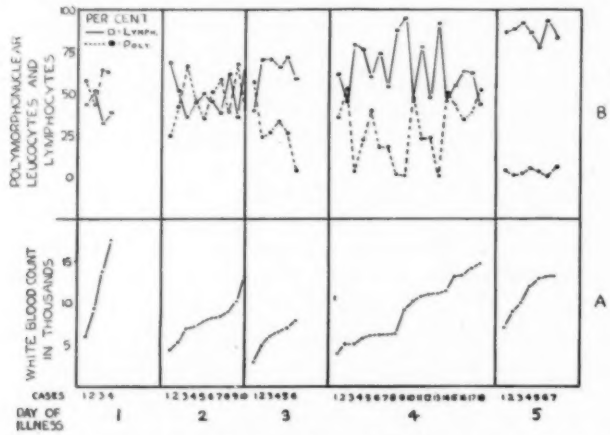

Fig. 5.—Correlation of white blood counts and differential counts in the first five days of roseola infantum. *A* reveals the falling of the white blood count to leucopenic levels by the third day and the return of the white blood count to normal levels by the fifth day of the disease. *B* reveals the decrease of the polymorphonuclear leucocytes and the rise of the lymphocytes as they occur in the second, third, fourth, and fifth days of roseola infantum.

VIII. DIAGNOSIS

The following example reveals the usual course of a case of roseola infantum:

L. K., a white male infant, aged 10 months, became suddenly ill on March 8, 1944, with restlessness, anorexia, and fever of 100° F. The infant was well nourished and well developed and had always had good care. No known exposure to any illness was forthcoming. In the evening of the same day the temperature rose to 104.6° F. and the patient became quite irritable and cried and whined as if in pain. On the morning (10 A.M.) of the second day, March 9, the temperature was 101.8° F., and the patient appeared slightly improved. Physical examination revealed a cross, uncooperative infant with few physical findings except slight congestion of the fauces and pharynx and both tympani. No nuchal rigidity or bulging of the anterior fontanel was made out. Slight enlargement of the occipital lymph nodes was palpable. Coryza or cough was not present. The heart and lungs were

essentially negative. The abdomen was soft. A cellular examination of the blood revealed the white blood count to be 10,000 per cubic millimeter with 65 per cent polymorphonuclear leucocytes and 34 per cent lymphocytes. The red blood count and hemoglobin were normal. A urinalysis was normal. The temperature reached 104° F. the evening of the second day, at which time the patient was very peevish and restless. His mother stated that he had not slept well for two nights. There was no night sweat, no cough, no vomiting, or diarrhea. On the morning of the third day the patient's temperature was 100.8° F. and his irritability was extreme. The general physical examination revealed palpable and apparently tender occipital lymph nodes, slightly inflamed fauces, tonsils and pharynx, and mild flushing of the eardrums. No Koplik's spots were present. Another white blood count and differential count was obtained and this time on the third day of fever a different picture was present. The white blood count was now 4,300 per cubic millimeter, and the polymorphonuclear cells were 29 per cent and the lymphocytes 70 per cent. In other words, a leucopenia with a relative decrease of the polymorphonuclear leucocytes had occurred. For three days he had refused his usual intake of nourishment, had not rested well, and was not his usual jovial self. Because he cried when pressure was made on his abdomen, his parents questioned whether he had swallowed some foreign body, and this they thought to be the cause of his irritability and abdominal distress. Their diagnosis, they believed, was enhanced by the fact that the infant had been constipated for three days. The rectal temperature on the evening of the third day was 102° F. The next morning (the fourth day) the temperature was 100° F. and the patient was less fretful. He drank more fluids. He wanted to play a little. That afternoon discrete pinkish macules from 2 to 4 mm. in diameter were seen on the lower abdomen and back. In the evening the lesions had spread to the chest and neck, with a few on the upper and lower extremities. The temperature was 99.4° F. at 10 P.M. on March 12, 1944, the evening of the fourth day. As the eruption began to make its appearance the infant's deportment improved and this same fact was noted consistently throughout the entire series of cases. On the fifth day, March 13, the exanthem was at its height and was present over the chest, abdomen, back, neck, and upper parts of the extremities. In some areas, especially of the abdomen and back, the lesions were confluent. Pinkish maculopapules were interspersed with the macules. No pruritus was evident. The injection of the ears, fauces, tonsils, and throat had subsided. The occipital lymph nodes were still palpable but were not tender. The child's appetite had begun to return, and in the evening of the fifth day he slept well. By the morning of March 16 (the eighth day) almost all of the exanthem had faded. All irritability had left and the parents believed their son to be normal again. No sequelae or complications were noted except that the normal appetite did not return until March 17. Treatment throughout the illness was directed toward alleviation of the symptoms.

Thus, from this case cited, it can be seen that roseola infantum is a disease entirely distinct from measles, German measles, and scarlet fever, three illnesses with which it is frequently confused. The sequence of events: fever for three to five days, followed by a macular or maculopapular exanthem accompanied by normal or near-normal temperature, and then convalescence with no complications or sequelae, mark it as a disease apart. The unexpected and sudden onset of fever

in a child under the age of 32 months presenting few physical findings commensurate with the high fever and irritability should make one think of roseola infantum in the pre-eruptive stage. The appearance of a macular or maculopapular eruption having a predilection for the abdomen, back, chest, buttocks, upper parts of the extremities, and with relatively few lesions involving the face, accompanied by slight enlargement of the lymph nodes, with blood findings presenting a leucopenia with a relative neutropenia and lymphocytosis should confirm the impression of roseola infantum.

Recurrence of the disease and even the illness without the rash has been described. It has been our experience also to have seen cases of each. Patients not revealing the eruption have findings typical of the disease, including the blood count. Doubtless many such cases are unrecognized unless one considers roseola infantum. Zahorsky has described this as being roseola sine eruptione. Many writers in their reports have remarked on the presence of similar cases.

Cases of roseola infantum in more than one member of the family within very short periods of time are unusual, but we have had three such occurrences. Following is a report of roseola in siblings:

K. C., aged 19 months, who had always been in good health, began to have fever of 101.8° F. accompanied by irritability on March 8, 1944. For the next two days there was no letup in the fever. Peevishness and anorexia were constantly present. Examination on the second day of the illness revealed pharyngitis and follicular tonsillitis as well as acute bilateral catarrhal otitis media. Slight enlargement of the occipital nodes was constantly present. On the fourth day of the disease a morbilliform rash made its appearance on the back and later spread to the chest, abdomen, and extremities. The temperature was normal when the eruption appeared. Two months later the patient had an attack of measles.

P. C., aged 33 months, sister of K. C., became ill with fever of 103° F. on March 11, 1944, three days after her brother first developed fever. After three days of fever she broke out in a generalized roseola save for the face and the lower parts of the extremities. The eruption was at its height for two days and then faded quickly. The lesions were thick on the buttocks. At no time was the child acutely ill. On the third day of the illness, examination revealed a mild follicular tonsillitis, similar to that of her brother. A white blood count and differential count revealed the typical findings of a leucopenia with a relative neutropenia and lymphocytosis. Coryza, conjunctivitis, cough, or Koplik's spots were never present. On May 20, 1944, two months after the attack of roseola, this patient had a typical case of measles. The eruption of measles appeared confluently on the face and chest in contrast to the disposition of lesions of roseola infantum which were present for the most part on the chest, abdomen, back, and buttocks.

IX. TREATMENT

No specific therapy is known or is necessary, so that treatment is entirely symptomatic. If the diagnosis is strongly suspected in the pre-eruptive stage then the treatment may be directed toward allevia-

tion of the symptoms of fever and malaise by the use of acetyl salicylic acid and phenobarbital in appropriate doses. An adequate diet and intake of fluids should be maintained. Sponge baths have a soothing and antipyretic effect when the fever is 103° F. and over. Medication with sulfathiazole or sulfadiazine neither relieves any of the symptoms nor alters the course of the illness. The pharyngitis, tonsillitis, and catarrhal otitis media clear up just as quickly without the use of sulfonamides.

SUMMARY

1. A study of eighty cases of exanthem subitum (roseola infantum) is presented.

2. Forty-two cases (52.5 per cent) occurred in boys and thirty-eight (47.5 per cent) in girls, revealing an almost equal distribution between the sexes. Most of the cases occurred during the months of February, March, April, and October.

3. The illness is a self-limited acute febrile disease of unknown etiology of infants and young children and is characterized by an abrupt onset, malaise, and termination in an afebrile exanthem having a predilection for the trunk, neck, and extremities. Fever, irritability, slight lymph node enlargement, and lack of findings commensurate with these symptoms are typical in the pre-eruptive stage. Sequelae or complications are very rare.

4. Peripheral blood findings reveal a relative leucopenia and neutropenia with lymphocytosis by the third day of the disease.

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INTESTINAL HERNIA WITH EVERSION AND EXTROPHIC BLADDER

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IN JANUARY, 1944, a 6½-pound, premature infant was born with a defect of the ventral wall extending from the umbilicus to the anus. The defective area was a red mucosal surface varying in depth of color in distinct patches. The herniation of the umbilical area was at first not large and protruded caudally through the extensive and thin-walled umbilical cord where it became continuous with the body wall. The child, whose death was expected at any time, continued to live and grow a little. After a month the child became very restless, cried a great deal, and lost weight. The umbilical herniation then developed into a long tube. The infant was taken to the Children's Hospital at Galveston at the end of two months and lived until the middle of April, dying of dehydration and emaciation with a weight of 5¼ pounds. The terminal temperature was 103° F.

At autopsy the head, chest, and upper abdomen showed no abnormality. The liver was small, weighing 80 Gm., but sections showed well-defined liver cords with large cells and compressed sinusoids. The spleen showed some, but not excessive, blood destruction. The vascular system was normal. Kidneys and ureters showed no sign of infection in spite of the fact that the ureters opened directly to the body surface in folds of the areas marked in Fig. 2. New glomeruli were in process of expanding under the capsule. The ileum passed into the hernial sac along the tubular extension for three inches. It was then everted. Despite its exposure the surface of this tube still showed mucosal structure with transverse villi and a fair amount of epithelium. Glands were intact. Where epithelium was missing the mesoderm flattened and built up intercellular matrix. From the open end of the ileum yellowish fecal material appeared with every peristaltic rush. The ileum was 56 inches long to this point and yet a generous intake of liquid food did not prevent dehydration. A small transverse mesentery in the sac carried a mesenteric artery laterally to each wall as the remnant of the omphalomesenteric arteries over the yolk sac.

There was an anal, or proctodeal, pit in the skin but no opening to the rectum. Instead, there was a 3-inch blind tube attached to this pit passing inward along the dorsal wall as a rectum and then looping downward to open in a long slit not far from its origin. The surface of the body here was thrown into large folds and was lighter in color than that of the ileum. It was sharply delimited from the middle of

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the hernial sac, whose epithelium, while red like that of the ileum, had low conical villi. The everted colonic area had typical mucous glands and crypts without villi and a heavy laminated smooth muscle wall. The lumen of the colon was empty except for a few desquamated cells.

Fig. 1.—Intestinal and urinary extrophy.

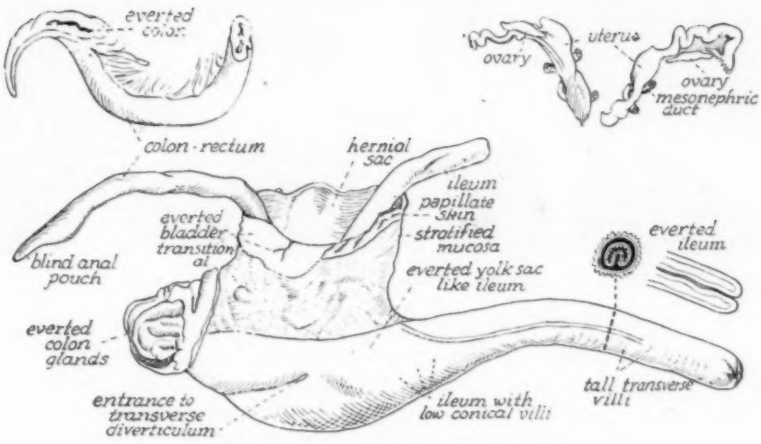

Fig. 2.—Herniated ventral wall in an infant.

The broad tubular entrance to the hernial sac was covered by a mucosal type of stratified squamous epithelium thrown into hillocks. It was easily distinguishable grossly and in section from the skin which bordered it above and also from the areas on either side on which thick transitional epithelium and thick loose bundles of smooth muscle disclosed the extrophied bladder.

On both sides of the colon, where it looped against the ventral wall, were a pair of uteri and tubes appearing to end blindly. Dorsal to these uteri were coiled mesonephric ducts. The ovaries showed cortical development normal for this age. A microscopic examination of the everted colonic wall showed that internal to this wall were a pair of tubes, possibly vaginal, opening into the deep folds and lined by stratified squamous mucosa like that outside. Between these tubes were a number of small cystic mucous glands and one trabeculated gland with epithelium like that of seminal vesicles.

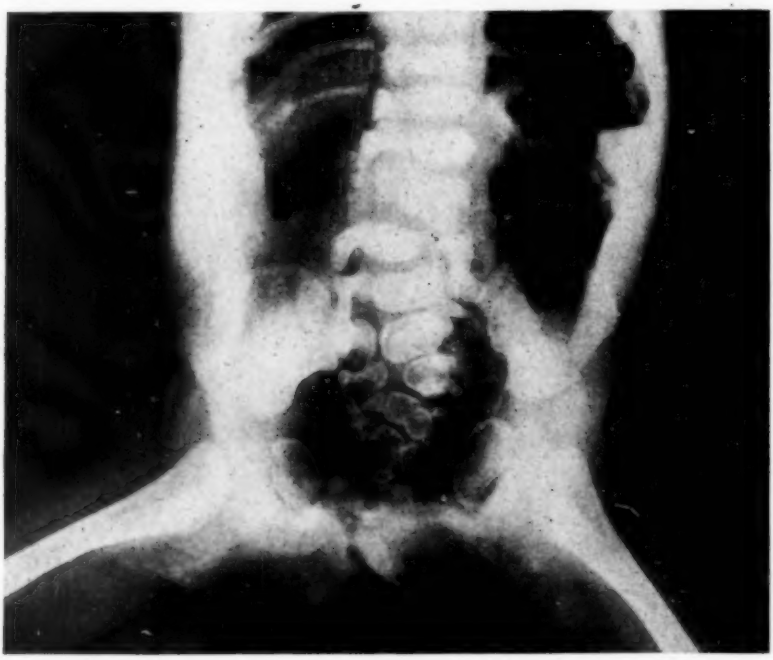

Fig. 3.—Lumbosacral defect.

A radiograph (Fig. 3) of the lower trunk shows that the defect was present in the lower thoracic region with eccentric development of the centra and lower ribs, though all were present. Lumbar vertebrae were compressed and the lower one, of the three which developed, was dislocated to the right. The whole vertebral column here and in the sacrum described a sigmoid curve. Pelvic bones were present but the pubes did not meet ventrally. The lower limbs were normally constructed but the foot was drawn into a pes cavus.

The origin of this defect goes back at least to the first formation of the ventral wall and perineum. There was a failure to narrow the umbilical duct and yolk stalk and to separate the latter from the uro-

genital sinus and allantois. The wall of these sacs then opened into and finally through the caudal wall of the forming umbilical cord.

The etiology of defects in development is shrouded in mystery since, in cases like this, genetic mechanisms are not clear and no external factor is evident. The fact that a genetic factor is at work is strongly indicated from the frequency of association of defective development in families in which they occur. This family is no exception. Both parents are normal and in their early thirties. They have two normal children. The mother, however, has in her immediate family two congenital defective relatives not resembling this infant. In a careful examination at autopsy it is commonly found that defects are associated in groups, some requiring microscopic study. The present autopsy was permissive and limited. Murphy[2] indicates that one defect in a family raises expectation of a second, to twenty-four times that of the general population. There are many exceptions. I have found lumbosacral defects in three out of four littermates among dog pups. Madero Bader, veterinarian of Galveston, told me that defective development is prevalent in particular breeds of dogs, among them the Boston bull terrier. These defects, when they appear, commonly include at least one-half of the litter and they may skip a generation or more. Dr. L. C. Dunn of Columbia University, in correspondence, stated that taillessness in mice has been found correlated with cloacal retention and an imperforate anus and this complex is gene determined. A previous case of lumbosacral defect reported by Sinclair and associates[3] is correlated quite differently with neuromuscular defects.

Studies of defective development with a gene basis, however obscure, should interest physicians who are to instruct parents concerning the probable normality of future children. It is true, as Haldane has pointed out, that sterilization programs or voluntary limitation has small eugenic effect on the population in the case of rare recessives, but its effect must be admitted in the prevention of misery in families where the expectation is high.

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TRAUMATIC RUPTURE OF THE SPLEEN

With Especial Reference to Its Characteristics in Young Children

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IN A report in 1932[1] on two cases of traumatic rupture of the spleen successfully operated on under spinal analgesia, the following factors were stressed:

1. Rupture of the spleen should be suspected in all cases of trauma to the abdomen since it is encountered in about 30 per cent of all such injuries.

2. The diagnosis is based on the history of abdominal trauma, signs of shock or internal hemorrhage, pain in the left hypochondrium radiating to the left shoulder, muscular rigidity, dullness in the flanks, nausea, and vomiting.

3. Increasingly persistent left upper abdominal pain after trauma to the belly even without external evidence is highly presumptuous of a ruptured spleen.

4. Shock and hemorrhage is best controlled by blood transfusion.

5. The management of ruptured spleen is surgical with splenectomy as the procedure of choice.

6. Low blood pressure does not contraindicate spinal analgesia in internal hemorrhage. On the contrary it renders the spleen more accessible and facilitates exploration.

Although since that publication the average annual admission of patients with trauma was 975, we have seen in the hospital a large number of patients with ruptured hollow and solid viscera, but up to 1943, a period of eleven years, not a single instance of rupture of the spleen, when in the course of a short period three such cases were referred. These were without exception young children in whom scout x-ray films did not show fracture of the ribs, yet the diagnosis of ruptured spleen was proved correct on operation. These experiences offer interesting points of observation to which I will refer after their presentation.

SURGICAL TECHNIQUE

The operative steps pursued in the series were as follows:

Our first care was to combat shock and internal hemorrhage by transfusion of plasma or whole blood both before and after operation. The abdominal cavity was exposed by a high left rectus incision. Any accumulated blood clots were gently mopped up, the colon was drawn down, and a large gauze sponge soaked in hot normal saline solution

From the Surgical Service, Edgewater Hospital.

placed behind the spleen. This last measure brings the viscus into good view and toward the surgeon's hands, thereby facilitating both observation and manipulation.

If examination revealed that the spleen had a simple, superficial tear, two or more mattress sutures were inserted to approximate the wound lips. This was followed by a continuous suture of fine catgut direct through the capsule to insure perfect hemostasis.

If, however, inspection revealed that the tear of the spleen consisted of numerous fine fragments, or the blood vessels themselves were torn, splenectomy was the indicated procedure. For this operation it is advisable first to clamp the splenic artery and to inject about 1 c.c. of adrenalin in order to enable the spleen to become contracted and emptied of its blood, which is thrown into the circulation as a supportive measure. It is only then that the pedicle should be clamped and the spleen removed in the classic manner.

CASE REPORTS

CASE 1 (57156).—On July 27, 1943, a boy 3½ years of age was brought to Edgewater Hospital by his physician with a history of having fallen off a swing, followed by pain in the abdomen and vomiting.

The pale and irritable child revealed a pinched facies. The abdomen was rigid, tenderness being marked in the left upper quadrant; pulse, 120 and weak; temperature, 100.6° F., respiration, 36 and rather shallow. The extremities were cold and clammy. Immediate blood count showed 3,600,000 erythrocytes, 10,400 leucocytes with 75 per cent neutrophiles and 25 per cent lymphocytes. The hemoglobin count was 80 per cent.

Scout x-ray films revealed neither gas beneath the diaphragm nor fractured ribs. With the diagnosis of rupture of the spleen the boy was given a transfusion and operated on five hours after his admission. After the removal of a large amount of free and clotted blood the spleen was seen to have a single large tear extending down through the entire viscus to the hilus. Conservative suturing as described in the preceding section was carried out and the abdomen closed without drainage. His blood count the following day showed 4,150,000 red cells with 90 per cent hemoglobin. The boy made an uneventful recovery and was sent home on the ninth postoperative day.

CASE 2 (58374).—A 7-year-old girl was brought to Edgewater Hospital by her physician at about 1 A.M. on Oct. 19, 1943. She had fallen out of bed on her abdomen and complained of nausea and severe pain in the upper part of the abdomen and left shoulder. She had an anxious facies; her pulse was 100; temperature, 99° F. Palpation revealed upper abdominal tenderness, some distention, and slight rigidity.

X-ray examination revealed a shadow over the left upper abdomen but no fractured ribs. Laboratory findings were: 4,170,000 erythrocytes; hemoglobin, 95 per cent; 7,150 white cells, of which there were 68 per cent polymorphocytes, 29 per cent large lymphocytes, and 3 per cent small lymphocytes.

A diagnosis of ruptured spleen was made and confirmed at operation, which clearly showed that the entire surface of the spleen had been ruptured, resulting in extensive intra-abdominal hemorrhage.

Splenectomy had to be resorted to. The spleen measured 10 by 4 by 2.5 cm.

While the child required several transfusions before and after operation, she made an uneventful recovery and was discharged after fourteen days.

CASE 3 (58425).—A 7-year-old girl was brought to Edgewater Hospital on Oct. 22, 1943, at 10 A.M. by the police with the statement that she had been struck by an automobile and thrown about twenty feet. The child was in severe shock and revealed contusions about the upper and lower extremities without any visible evidence of injury to the chest or abdomen. Her face and head showed some bruises. She complained bitterly of pain over the entire abdomen which was extremely tender to the touch and very rigid. Her pulse was 130, respiration, 32; and her facial color, ashen gray. Scout films were made at an early moment with negative findings. The bladder was catheterized and microscopically revealed blood in the urine.

A diagnosis of ruptured spleen with internal hemorrhage was made and the patient taken to the operating room after treatment for shock by a hypodermic injection of morphine and the administration of blood plasma.

During operation the patient's blood was typed and she was given a transfusion of 500 c.c.

On exposure the abdominal cavity was found to be filled with blood and the spleen was seen to be torn into two halves and some shreds, necessitating splenectomy. Immediately after completion of the operation another transfusion was given, less than two hours after the girl's admission to the hospital.

The pathologic report revealed the spleen to be in two halves and shreds totally measuring 4 by 5.5 by 3.5 cm., with a recent blood clot in each of the opposing surfaces.

A blood count taken immediately after admission showed 3,900,000 erythrocytes with 72 per cent hemoglobin, 14,200 leucocytes with 80 per cent neutrophiles and 20 per cent small lymphocytes. A comparative blood study made three days later revealed 3,790,000 erythrocytes with 73 per cent hemoglobin, 12,700 white cells with 80 per cent neutrophiles and 20 per cent small lymphocytes. Six days after admission and as the result of a third transfusion the red cells numbered 4,650,000 and the hemoglobin had risen to 96 per cent.

The microscopic appearance of blood in the urine continued until October 25, which substantiated the operative diagnosis of contusion of the left kidney made on the presence of a retroperitoneal hemorrhage.

The little patient made a complete recovery and was discharged home on the tenth postoperative day.

COMMENT

Careful perusal of the foregoing case reports will unquestionably support the points stressed in my first article[1] on the subject of traumatic rupture of the spleen and cited in the introductory part of this communication. It is seen that all patients in our series were children not above the age of 7, and that in no instance was there any visible evidence of injury to the chest or abdomen, nor did x-ray films show

the presence of fractured ribs, which under like conditions would be the case in many adults.

Nevertheless, a prompt diagnosis of splenic rupture was made and immediate surgical intervention saved the lives of the unfortunate children. It may appear rather bold to operate on a child on the assumption of the presence of internal hemorrhage when the blood examination showed no appreciable reduction of the number of red cells and of the percentage of hemoglobin, but the findings after opening the abdomen have shown the wisdom of not relying on the blood study for a diagnosis of internal hemorrhage, a point of importance to which we will revert in the next section.

The experienced surgeon needs only the history of regional trauma, the hippocratic facies and the other somatic evidence of shock plus the muscular defense to recognize the presence of hidden hemorrhage. Accordingly the immediate institution of measures to combat shock and laparotomy to control the hemorrhage and deal with the lesions is the only safe course to pursue.

Granted for the sake of argument that occasionally a diagnosis of ruptured spleen may prove erroneous, the therapy certainly will not be wrong for invariably one will find some important lesion with loss of blood elsewhere in the abdominal cavity.

The circumstance that x-ray films have failed to show fracture of ribs in any one case of our series raises a question which has occupied the minds of many investigators. It is conceded a priori that in young children the resilience of the cartilaginous ribs reacts to external force by a temporary displacement without a break in the continuity of the ribs. This, however, raises the corollary regarding the modus operandi by which the spleen sustains rupture.

Many investigators have assumed that because the spleen is usually ruptured at the hilus and the viscus is suspended by a pedicle the tearing must be attributed to a sudden intra-abdominal force directed against the hilus, somewhat like the tearing of an umbrella by a sudden gust of wind or like a paper bag bursting by sudden compression. While theories of that type seem plausible, it is my conviction that in most instances the spleen becomes ruptured through direct violence. I submit the biologically reasonable thesis that the ribs are suddenly compressed over the spleen and cause a lesion at the weakest point, the hilus, or split the surface (periphery) of the spleen into one or more fragments. Naturally after the injury the ribs spring back into their original position without themselves having sustained a fracture.

It is true that in adults the ribs are broken in about 10 per cent of cases of splenic rupture, but in the five more or less typical cases in our series no such injury was evidenced.

The theory of intra-abdominal pressure change becomes untenable when one takes into consideration the great number of abdominal concussions, injuries from blasts or explosive missiles in war. In such cases

neither operation nor autopsy has revealed splenic rupture, the injury being usually confined to small rents in various viscera or pin-point hemorrhages. Of course we do not include crushing injuries which offer the exception. Let us further consider the question why prize fighters doubling up with pain after blows to the solar plexus or other men engaged in athletic sports sustaining similar traumas do not more often show rupture of the spleen. One sees again and again injuries of a degree severe enough to rupture the urinary bladder, the intestine, the mesentery, and other viscera, yet the spleen remains intact. In such cases we have the very best examples of sudden change in intra-abdominal pressure, yet the spleen remains unaffected.

For these reasons there remains the sole logical assumption that the spleen is injured solely when that organ lies in a direct line of violence or is struck directly by the elastic ribs of the young after a fall, blow, kick from a horse, auto or railroad collision.

Parenthetically it is pointed out that the theory here advanced is particularly applicable to spleens pathologically changed by malaria, typhoid fever, Banti's disease, and the like.

EVALUATION OF THE BLOOD COUNT

Attention has been drawn to the circumstance that the reduction of the red blood cell count and of the percentage of hemoglobin is not pronounced soon after the occurrence of an internal hemorrhage, a factor which may tempt some surgeons to assume a waiting attitude, when delay in prompt intervention may in many instances prove disastrous.

It is again emphasized that actual loss of blood and blood findings cannot be synchronized, at least not in the early phase of injury. Thus our case reports show on admission more than 3,500,000 red cells and more than 72 per cent hemoglobin, and it was only after a lapse of several hours that the hemoglobin fell below that percentage and the red cell count below 2,500,000. This phenomenon in all probability depends on one of the functions of the spleen as a blood reservoir or bank so that when it becomes contracted or crushed, a large part of the blood reserve is thrown into the circulation.

Here it may be interpolated that while commonly the spleen is not regarded as an organ essential to life, even if it has no other function than that just stated, it should be preserved whenever possible. It is for that reason that while we have acknowledged splenectomy to be the operation of choice, we have welcomed every chance to preserve the viscus. We refer back to the case reports for proof that in lesions of the spleen of limited extent and degree conservative surgery brings about a *restitutio ad integrum* and, as happened in our three of the five cases, complete recovery.

That the blood count should not be accepted as the sole criterion for or against immediate surgical intervention is best illustrated by a case

which was seen at Edgewater Hospital shortly after the publication of my previous article. This case which is not included in my series was managed by one of the hospital staff surgeons.

A 13-year-old boy (19076) was admitted to the hospital on May 31, 1932. His physician stated that two days before he had fallen from his bicycle over a hydrant striking his left side. There being no evidence of an external injury the boy was kept at home for observation, but became very ill, so that on admission a diagnosis of shock and internal hemorrhage was entered. His pulse was 116; respiration, 22; temperature, 100.4° F. Tenderness and rigidity were present over the upper quadrant of the abdomen. Scout films showed no fractured ribs. His blood picture on May 31 at 10 A.M. (that is, two days following the accident) was: 80 per cent hemoglobin, 5,200,000 red blood cells, 6,600 white blood cells with 75 per cent neutrophiles, 25 per cent small lymphocytes. The patient was not operated on until June 6 for internal hemorrhage. During this time his blood picture was as given in Table I.

TABLE I

DATE	HOUR (P.M.)	HEMOGLOBIN %	RED BLOOD CELLS	WHITE BLOOD CELLS
May 31	6	75	3,800,000	9,200
May 31	7	75	4,095,000	6,400
May 31	10	78	5,400,000	9,400
June 1		68	3,800,000	9,300
June 2		67	3,630,000	10,100
June 3		65	3,580,000	11,400
June 4		65	3,610,000	11,800
June 6		60	3,130,000	11,000

Operation on June 6 disclosed a belly full of blood, a rupture of the spleen and of a portion of the pancreas with active hemorrhage. The tail of the pancreas was ligated, the spleen approximated with interrupted mattress and continuous sutures of the capsule. The patient was given blood transfusions before and after operation. He was discharged after two weeks and a rather stormy convalescence.

This case serves to illustrate several points: (1) that the delay might have been fatal if allowed further to continue; (2) that this type of case should be operated on as soon as ruptured spleen or internal hemorrhage is suspected.

This case could be interpreted as one of delayed splenic rupture in which the acute abdominal insult does not manifest itself immediately and there is a latent period of hours, days, or weeks after the original injury. During this time the patient may not complain about his internal injury but instead may have some abdominal distress or pain from a fractured long bone or fractured ribs. Then he suddenly becomes acutely ill as in the foregoing case when collapse, shock, and severe anemia began to manifest themselves. Very often, if the hemorrhage is severe, death may ensue before laparotomy can be performed.

According to Zabinski and Harkins,[2] Harkins in 1943 collected 177 such cases from the literature and reported four of his own. That author states: "This condition with its original injury, insidious latent

period and fulminating secondary hemorrhage is the condition of delayed splenic rupture.'' It is, therefore, imperative that we remember not only the acutely ruptured spleen but the delayed ruptured spleen in every upper abdominal injury.

CONCLUSIONS

1. Fractured ribs are exceedingly rare in children when associated with ruptured spleen.

2. Reduction of the red cell count and hemoglobin does not take place as rapidly as one would expect with severe internal hemorrhage.

3. The history of a fall or injury to the left upper quadrant of the abdomen or lower chest with signs of internal hemorrhage and abdominal rigidity with or without external signs of injury warrant the diagnosis of ruptured spleen in children.

4. Immediate laparotomy and blood transfusions should be performed before there are very late findings of internal hemorrhage as recovery depends on the time of operation and amount of blood lost.

5. Although splenectomy is the operation of choice in most instances the spleen should be spared whenever possible as the organ serves a very useful purpose.

6. Delayed splenic rupture should be kept in mind in every upper abdominal injury in which the symptoms may be masked by the associated injuries.

7. Ruptured spleen in children is probably caused by a direct blow to the spleen transmitted through the upper abdomen by flexible ribs, the latter springing back into place with no signs of external injury.

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American Academy of Pediatrics

Proceedings

THIRTEENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

St. Louis, Mo., Nov. 9-11, 1944

EMIC SESSION

Opening Statement

Joseph S. Wall, M.D., Chairman of the Special EMIC Committee

THE first request for funds to care for wives of enlisted men came to the Washington State Health Department in the summer of 1941 from the commanding officer of Fort Lewis, who asked for assistance in obtaining maternity care for the wives of enlisted men at that post. In July, 1941, the Children's Bureau approved the project and made available certain funds under the provisions of Title V of the Social Security Act. The Conference of State Health Officers, meeting with the Children's Bureau in March, 1942, requested that the Bureau set aside a portion of the Federal funds available to the States to be used as grants for these special projects. By December, 1942, twenty-six states had initiated programs but did not have sufficient funds to continue them for more than a few months. The Children's Bureau then made an appeal to the Congress for additional funds for carrying out the project on a state-wide basis with the result that an initial special appropriation of $1,200,000 was made by Congress for the emergency maternity and infant care program, hereinafter referred to as "EMIC," in March, 1943. (J. A. M. A. **123**: 845, 1943.)

The wording of the Act establishing funds for the EMIC program is as follows:

"PUBLIC LAW 11—78th Congress. Grants to States for emergency maternity and infant care: For grants to States, including Alaska, Hawaii, Puerto Rico, and the District of Columbia, to provide, in addition to similar services otherwise available, medical, nursing, and hospital maternity and infant care for wives and infants of enlisted men in the armed forces of the United States of the fourth, fifth, sixth, and seventh grades, under allotments by the Secretary of Labor and plans developed and administered by State health agencies and approved by the Chief of the Children's Bureau, fiscal year 1943, $1,200,000." The language of the 1945 appropriation includes Army Aviation Cadets and provides 2½ per cent of the funds appropriated for State administrative purposes.

According to the statement of the Associate Chief of the Children's Bureau published in the October number of the JOURNAL OF PEDIATRICS (**25**: 358, 1944), at meetings of its advisory committees on Maternal and Child Health and Services for Crippled Children held in December, 1940, and in December, 1941, "Many problems related to the war were discussed as well as the long-time maternal and child-health and crippled children's programs and the need for their extension."

The last meeting of the advisory committee just quoted took place on Dec. 1 and 2, 1941.

According to the statement of the Associate Chief of the Bureau just quoted, the usual meeting of the Advisory Committee on Maternal and Child Health which would ordinarily occur in December, 1942, "was postponed until decisions could be reached by the Bureau of the Budget and Congress in regard to a deficiency appropriation to meet the requests of a number of state health agencies for additional funds to carry forward their programs of maternity and infant care for the wives and infants of enlisted men." (This would clearly indicate that EMIC was then in actual operation.) "Until the first Deficiency Bill for 1943, which carried the first appropriation for EMIC had been agreed to by both houses of Congress and approved by the President and until the full intent of Congress as to the purposes for which the appropriation could be spent was clarified in hearings and debate, the Children's Bureau was not in a position to discuss policies of administration profitably with either the advisory committee or the state health officers."

The statement of the Associate Chief says in a previous paragraph that "The Children's Bureau acted on a recommendation of the Conference of State and Territorial Health Officers meeting in March, 1942 (the previous year), when it set aside $198,000 of the 1943 appropriation to meet specific requests of state health agencies for funds to provide maternity care for the wives of service men and care of their infants." (This phrase by a shorter title spells EMIC.)

The Bureau records that, "On March 23rd, 1943, 23 state maternal and child health directors and several of the state health officers met with the Staff of the Children's Bureau to discuss in detail the proposed administrative policies; on March 25th, 1943, the usual annual conference of the State and Territorial Health Officers was held with the Children's Bureau."

Under date of March 29, 1943, there was issued by the Bureau the complete detailed structure of the EMIC program under the title, *MCH Information Circular No. 13.* Instructions to state health agencies "with regard to plans and financial reports related to Emergency Appropriations for maternity and infant care." This was a document of some twenty pages.

Finally, at long last, on April 6, 1943, "The Advisory Committee on Maternal and Child Health met and discussed the program and pro-

posed policies with the Staff of the Children's Bureau." The last previous meeting, as noted, had been on Dec. 1 and 2, 1941.

In this brief embryonal history of EMIC it would appear that the program was conceived in the crowded precincts of a camp on the shores of the Pacific in the summer of 1941, where prenatal care was given largely by State and Territorial Health Officers, State Maternal and Child Health Directors, together with the Staff members of the Children's Bureau. The program was finally delivered, after considerable dystocia, into the lap of the pediatrician (with obstetric consultation) on April 6, 1943, bearing all of the earmarks of prematurity and many of the handicaps incident thereto. There was lack of development, many congenital defects, some stigmata of degeneration and ageneration and even certain monstrosities which not only boded ill for a healthful life, but presaged rather a perilous existence during its early months. The pediatrician has never lacked in courage or patience in ministering to the wants of the premature, and so it was with EMIC. What were some of the ills from our standpoint?

Early and premature solicitation of wives through the medium of "stuffers" carried in pay allotment envelopes before adequate explanation of the plan to, and acceptance by, members of the medical profession; inadequate compensation for services rendered; excessive and annoying "paper work"; denial of supplemental fees from those who could adequately afford to pay the usual charges prevailing in the locality where services were to be rendered; refusal to allow supplemental funds to be used by the patients to secure better hospital accommodations in the interest of greater privacy with the mental comfort incident thereto; failure to divorce hospital care from medical care; lack of recognition of the services of superiorly trained pediatricians except upon a consultation basis; the directive that "Hospital outpatient department or health department clinics rendering satisfactory services for sick infants should be used whenever arrangements can be made for acceptance under the plan"; referral of all infants included under the program to child health conferences for medical supervision and immunizations; glaring omission of child health supervision as a function of the physician and not an exclusive one of public clinics (this has now been corrected by the adoption of recent policies by the Bureau). Numerous administrative directives which were productive of irritation and disgruntlement on the part of the medical profession and especially the insertion of a "middleman" in the patient-physician relationship.

This résumé but briefly outlines the genesis of EMIC throughout its early days; its inception hurried, its completion, through the necessity of haste and not to be ascribed entirely to the fault of its architects, containing some ambiguities and many points of irritation, but accomplished with remarkable dispatch considering the magnitude of the issue undertaken amidst the turmoil of unpreparedness.

There was in the building of the EMIC program one serious fault which fairness of analysis cannot deny, nor should it condone. The

foundation of the plan was conspicuous by the absence of what is now commonly known as "collective bargaining," that essential element of amicable relationship between management and labor, evolved through conference and understanding, between Federal and State administrators, on the one hand, and the actual "purveyors" of medical care in the field of direct application of services, on the other.

This glaring fault, productive of discord, disharmony, and even failure in laudable efforts toward medicosocial betterment, is not uncommon in propaganda as well as in actual accomplishment of so-called social gains.

Instead of the words "collective bargaining" with their implication of haggling, "collective agreement" would be the better term, for this phrase is quite synonymous with accomplishment, which is the desideratum to be reached.

To do less than to invoke "collective agreement" in medicosocial planning, to direct the terms and conditions of medical services rendered by physicians by Federal or State fiat, amounts actually to confiscation of property without due process, that property being the intellectual ability of the physician, who must not be reduced to slave labor by decree as is the practice in a Nazi or Fascist state.

Fortunately, many of the controversies enumerated comprise muddied water now passed over the dam, many have been solved, or are in the process of solution, especially by reason of the fact that in the past year (1943) the EMIC program has been subjected to "collective agreement" among members of the Academy, State administration officials, and members of the Children's Bureau Staff.

As a part and parcel of national legislation the EMIC program fell within the purview of the Committee on Legislation of the Academy and, more especially, engaged the attention of its chairman residing in the Nation's Capital.

The first cognizance the Academy took of appropriations for the care of servicemen's wives and infants was during the annual meeting in Chicago in November, 1942, when a resolution endorsing House Bill 7503 and Senate Bill 2738 was voted upon favorably, the report in the minutes stating that this action was taken "after considerable discussion."

The chronological history of efforts made by the Academy officers and committeemen and women has been published in the July number of the JOURNAL OF PEDIATRICS (**25**: 92-93, 1944). A brief review of the content of proposals made by your representatives to the Children's Bureau in conference and by communications might with advantage be recounted, especially in view of the fact that your representatives in their presentations of the viewpoint of the Academy had to rely on impressions and suggestions obtained by letter as well as by conversation with as many fellows and officials as could be reached in the absence of a general session of the Academy. Whether we have rightly interpreted

and correctly advocated the collective opinion of the Academy rests with you to decide.

On Nov. 6, 1943, the Executive Board requested the Children's Bureau "in order to obtain the high quality of medical service to which the wives and children of servicemen are entitled," to call, forthwith, a conference of official representatives of the servicemen, together with official representatives of the professions actually rendering this service; namely, the American Medical Association, the American Hospital Association, the United States Public Health Service, the American Association of Obstetricians and Gynecologists, and the American Academy of Pediatrics."

On November 16, prior to the meeting of the requested conference, representatives of the Academy met with the Associate Chief of the Bureau in Cincinnati at the time of the meeting of Region II in that city. Problems of health supervision were mainly discussed, the Chairman of the Committee on Legislation advancing the following proposals:

By implication, the intent of Congress to grant to the patient the right of free choice of her attending practitioner may be and should be construed to extend to the mother a choice of the one to care for her infant. We proposed to amend the first sentence of the second paragraph of page 5 of MCH circular of information No. 13, to read, "Infants included under this program may be referred to child health conferences for medical supervision and immunizations wherever arrangements can be made, *provided such arrangements are satisfactory to the mother.*" This wording was proposed as a substitute for that of the directive which read, "Infants included under this program should be referred to child health conferences for medical supervision and immunizations."

We proposed to amend 7 and 7a to read, "Where arrangements are not made for referral of infants to a child health conference for health supervision and immunizations, physicians who have been trained in pediatrics or who are otherwise devoting a majority of their practice to pediatrics and who have been trained in health supervision of infants may be paid for giving health supervision in their offices. An inclusive rate covering the infant's first year of life should comprise monthly office visits for health supervision, together with the usual immunizations." It was suggested that an "inclusive rate" not to exceed $30.00 should be established by each health agency on a state-wide basis for such services. The inclusion of minor ailments such as would be treated in the office within this inclusive fee was also discussed.

On Nov. 29, 1943, the Chairman met with the Associate Chief of the Bureau and Dr. Daily, then Director of MCH, presenting certain suggestions which were amplified by letter on November 30 to the Associate Chief of the Bureau, as follows:

"As a result of our conference of yesterday, I would like very much 'to place in the record' the following observations and opinions which, although they represent my own personal views, nevertheless, largely

reflect the opinions of the members of the Academy with whom I have discussed the subject.

1. The Academy believes in the policy of a direct grant of funds to the mother for her own care and that of her infant. This question, in view of the defeat of the Smith amendment on the floor of the House, has been decided in the negative and now governs the policy of the Children's Bureau. (By way of parenthesis, it is my belief that this Congressional policy should have been given greater and wider publicity in the beginning as such knowledge would have prevented a flood of criticism as the real reason for the Bureau's policy only came to light three days ago in the publication carried in the *Journal of the American Medical Association.* The only other explanation available to the medical profession before that date being the one voiced by a high official of the Bureau, namely, to quote, "If physicians participating in the program were permitted to charge the enlisted man's wife fees in addition to the payment received from the state health agency, there would, of course, be no way of preventing some physicians from charging their regular fee from the patient and collecting the fee from the State health agency. This would, of course, defeat the purpose of the program mentioned above. . . ." This blanket indictment of the profession has caused much resentment because of its attack on the integrity of physicians and accusations of probable avarice.)
2. Inasmuch as the question of including health supervision by pediatricians was uppermost in our minds during yesterday's conference, I feel that the following facts may be pertinent:
   Policy regulations concerning the application of the program to infant care should not be made solely nor even largely from the viewpoint of those adopted for maternal care nor should the attempt be made to equalize well-infant and sick-infant care with obstetric conditions to which they are not comparable.
   Regarding the question of an "inclusive fee" for health supervision by pediatricians and whether such fee should include the medical care of the infant during his first year if he became sick, it is my feeling that pediatricians would much prefer a separation of the compensation into two distinct entities, namely, health supervision of the infant and care during illness, the first element being placed upon an inclusive fee basis while the second should be paid for under the regulations and fees now established, or to be established, by the Children's Bureau. Pediatricians, together with other members of the medical profession, are opposed to the blanket policy of attending the sick on a fixed, inclusive fee basis partly because of the hazards involved in undertaking such unpredictable con-

ditions of sickness so far as medical attention is concerned, and, furthermore, as they almost unanimously abhor such a method of "group" practice because of the principle involved. On the contrary, health supervision care during the first year on a fixed fee basis is a custom which prevails throughout many states and has proved satisfactory because the expenditure of time and professional skill is predictable. This is the only part of the pediatric care program which I believe may be placed upon a comparable basis with obstetric care and, if adopted by the Bureau, I think the comparison should be made equitable with the provisions now prevailing in regard to compensation for prenatal care, namely, six prenatal visits for an inclusive fee of $15.00.

If you remember, when Dr. Daily stated that six visits during the first year would be an adequate number for health supervision, I immediately challenged his opinion, for such is not the experience nor the practice of pediatricians. At least monthly visits, for they would include immunizations, should be provided for adequate health supervision and if such a plan should be adopted by the Bureau, the thought should be carried in mind that this care is to be given by pediatricians or by those experienced in giving such care, not by general practitioners, osteopaths nor midwives, who, with others, are now unfortunately by act of Congress permitted to embrace prenatal care and are compensated at the rate of $2.50 per visit.

It is my belief that the fees mentioned at yesterday's meeting, namely $18.00 for eight health supervision visits to the office are inadequate and unacceptable to pediatricians. That monthly visits for such supervision at an inclusive rate of $30.00 (including immunizations) would be fair and equitable and more comparable with prenatal care on the obstetric side, if such comparisons are to be taken into the equation, of which I doubt the propriety. That what one might call "accidental" sickness during the baby's first year may involve extraordinary attention by way of administration of elyses, transfusions, and other procedures far beyond the "accidental" sickness during the prenatal period. That the care of the sick infant should be entirely separated from health supervision and compensated for in the manner now prevailing.

3. In regard to the compulsory utilization of child health conferences I must still personally disagree with this directive of the Children's Bureau, notwithstanding the interpretation of its solicitors as expressed in the bulletin of March 29, 204, Sec. 2 which carries the clause, "for whom similar care is not readily available from the medical or hospital facilities of the Army or Navy or from facilities provided by or through official state

or local health agencies." Public Law 135 distinctly states on page 4 under "Grants to states for emergency maternity and infant care (National Defense) . . . TO PROVIDE, IN ADDITION TO SIMILAR SERVICES OTHERWISE AVAILABLE, etc." . . . It may be permissible for us each to have contrary opinions!

4. Finally, I feel that it would be unwise and incompatible with that cooperation of pediatricians which the Children's Bureau has always desired and which it has heretofore received, to promulgate and publish new regulations regarding the administration of the funds for care of servicemen's wives and children, which, of course, it has every right to do, without calling first the conference requested by the Executive Board of the Academy of Pediatrics as outlined in the resolution adopted by the Board on November 6. Surely, the present regulations now in force, together with the explanatory statements contained in the *Journal of the American Medical Association,* published three days ago, should obviate the necessity of promulgating revised regulations without considered discussion with those who have requested a hearing and whose aid is to be sought in carrying out the program proposed."

On December 10, and 11, 1943, the conference requested by the Executive Board was held in the Children's Bureau, the Chairman of the Legislative Committee of the Academy making the opening statement in its behalf, which, in part, comprised the following observations:

"The purpose of the conference is to present to the authorities certain objections to the present regulations governing the administration of the (EMIC) act, more especially because new regulations are in the process of formation and to request modification and change in many regulations now operative." "It is the feeling of many physicians throughout the country that, although not so intended, if this experiment in state medicine is to be interpreted as a "trial balloon" with implications of future trends of federal participation in medical practice, let this lighter-than-air-craft have not only a Federal pilot but also a co-pilot from that profession which alone can apply the principles of health care involved and without the cooperation of which, a crash landing becomes inevitable."

Your representative, together with the official delegates from the American Medical Association, advocated cash allotments to the wives of servicemen as well as the supplemental use of the patient's own resources, including hospital insurance funds, to secure (1) more highly qualified obstetrical care and (2) more privacy in hospital accommodations. The objection was made that "the limitation of fees for obstetrical care and delivery will cause many highly qualified physicians to avoid taking part in the "panel" and will no doubt relegate the care

of many wives to the questionable practices of ignorant and incompetent practitioners, more especially because the law now states that such persons must not be discriminated against." The fee was then $35.00.

Strong objection was made to the omission of child health supervision (except in clinics) and the implied desertion of the principle of keeping the well child well, as a function of the physician, a doctrine developed by pediatrics and always furthered by the Children's Bureau.

Under date of Dec. 23, 1943, the following communication was addressed to the Associate Chief of the Children's Bureau:

> Dear Dr. Eliot:
>
> Many thanks for your letter of the fifteenth inst., and for your frank expressions it contained.
>
> I regret that because of the size of the recent conference and the great number of generalities under discussion, the opportunity was not afforded to more intimately consider with the obstetricians and pediatricians the specific problems involved with a view to their solution, which proved rather impracticable because of the diversified interests represented at the conference.
>
> I share with you great concern over the reaction experienced by pediatricians (as well as by many practitioners of medicine) as a result of this initial participation of government in medical practice and believe that the impasse has largely been created by the denial to physicians of that security guaranteed by one of the Four Freedoms, namely, "Freedom from Fear." This fear of the future of their profession, of the jeopardy to the ethics and standards which have governed medical practice during the past, and the disinclination of the American mind to accept government by regimentation and official fiat, have all contributed to the disgruntlement, resentment, and actual antagonism which now seems to pervade a large segment of the medical profession, as reflected in the comments which have come to your attention and to mine.
>
> I am exceedingly anxious that the new regulations for the conduct of the EMIC plan will reflect some of the requests and recommendations urged by so many pediatricians, which may go a long way toward securing that good will and cooperation which we both so much desire on the part of our colleagues.
>
> In my opinion, it would be of tremendous importance in bringing about a better understanding, if the Children's Bureau could see its way clear to promise the members of the medical profession that in future congressional hearings in justification of continuing or additional appropriations, the opinion of the medical profession as to the granting of cash benefits to the wives and for the care of infants of servicemen be adequately presented to the committees, even if the administrators of the plan may disagree with the principle involved.
>
> That every effort be made to include in the new regulations some plan for the return of infant health care to pediatricians and practitioners qualified to undertake health supervision, rather than to relegate this most important safeguard of infant welfare to clinics of state and municipal health agencies. Even

if it now seems difficult to include in the regulations an inclusive payment health supervision plan, some provision might be made that infants possessing potential or actual nutritional evidences of failure of proper growth and development might be extended medical care in the same category as that of sick infants, which they are likely to become, unless measures of health supervision are employed promptly. Exactly how such evaluation of failure of satisfactory progress on the part of the infant is to be made in the absence of monthly health conferences with a physician, is a bit of a problem, but the solution might lie in having the public health nurse determine through her home visits those babies who are in need of health supervision by a physician, to whom she may make the necessary certification for care and treatment.

I trust it may not be considered presumptuous on my part to make these suggestions but my reappointment to the Advisory Committee of the MCH division of the Bureau and my relationship to the Academy of Pediatrics have emboldened me so to do. I assure you that I shall be glad to confer with you any morning in the near future which you may find convenient, should you so desire.

With all good wishes of the Season, believe me,

Sincerely,

JOSEPH S. WALL.

As a result of the December meeting, the Children's Bureau on Feb. 1 and 2, 1944, called a special conference of pediatricians, state health officers, and maternal and child health directors to discuss child health supervision, the value of child health conferences, and the ways and means of providing health supervision of infants under EMIC. The conference discussed:

1. What plans should be made for the future expansion of child health supervision of the best quality throughout the country?
2. How can child health supervision be made available (of the best quality) under the Emergency Maternal and Infant Care Program?
3. Should public health agencies finance child health supervision in physicians' offices as well as in child health conferences?
4. Methods and rates of payment to physicians for child health supervision.
5. Training and experience necessary for child health supervision.

On Feb. 28, 1944, President Franklin P. Gengenbach notified me that he had been appointed Chairman of a Special Committee for Cooperating with the Children's Bureau with Regard to the EMIC Program, since which date this Special Committee has represented the Academy in its relations with the Bureau. The absence of the chairman as delegate to the Mexican Congress on Pediatrics caused some delay in gathering material for the use of the committee but throughout April and May, by letter, by questionnaire, and by a conference with the State Chairman of Region I held in New York, material was in hand for a

meeting of the committee on June 8, 1944, just preceding the meeting of the Executive Board. Members present were Allan M. Butler, Alice D. Chenoweth, Martha M. Eliot, Julius H. Hess, Lee Forrest Hill, Joseph I. Linde, Stanley Nichols, and Borden S. Veeder. Edward B. Shaw of California was unavoidably absent.

The deliberations of this conference, lasting from 10 A.M. to midnight, while not opened with prayer by the chairman (although that thought lingered in the subconscious mind), were initiated by reading a quotation from Voltaire, to wit: "I wholly disapprove of what you say but will defend to the death your right to say it," a bit of wisdom from that famous Frenchman who believed neither in prayer nor in doctors!

The principle of "collective agreement," heretofore mentioned as necessary to the satisfactory solution of controversial problems, dominated the interchange of many divergent thoughts and marked the beginning of better understanding and more productive cooperation between the Academy and the Children's Bureau, which has continued uninterruptedly to the present time, and which, in my mind, should be acclaimed with satisfaction by the membership of the Academy not only because this spirit marks the accomplishment of certain desired goals, but because it is a harbinger of still greater accomplishments in the future in mutual endeavor to attain our common objective, the best that pediatrics can contribute to the welfare of our children!

One of the main subjects for the consideration of the committee was the analysis of a questionnaire containing fifty-eight questions which were propounded to all Regional and State Chairmen. Thirty-nine replies were received, not all in time to be included in our discussion. Upon the agendum of the meeting also appeared the following items:

1. That the Children's Bureau cease and desist from its opposition to the change in methods of administering the funds of the EMIC Program from the present method to that of a cash grant to the wives of servicemen (the vote of the questionnaire was two to one in favor of such a change).
2. That health supervision of EMIC infants during their first year be permitted in the offices of pediatricians and properly qualified practitioners.
3. That the Children's Bureau withdraw its directive that EMIC infants be given health supervision only in conferences "made available by state or local health agencies or by voluntary health agencies."
4. Again establish in the Bureau's regulations a fee differential for pediatricians and general practitioners.
5. Modify the regulation appearing on page 3 of EMIC Information Circular No. 1, which states, "Individuals accepted for care under the program will be referred routinely to local public health agencies for the provision of public health nursing services that can be made available."

6. Reduce paper work to a minimum.
7. Remove the discrimination against pediatricians in the present regulations whereby the highly qualified pediatrician (whose qualifications are set forth) is compensated at the rate of $2.00 a visit, while his colleague, the general practitioner, without such high qualifications in infant care is remunerated at the rate of $3.00 per visit.
8. Withdraw from circulation and suppress Folder No. 31. If reissued, eliminate (1) reference to the quality of care in the clinic as being superior to that given by a doctor in his office; (2) eliminate the repeated dictum that the clinics should be free to all comers, irrespective of financial status.
9. That the Children's Bureau permit the state health agencies, as directed by law, to develop EMIC plans, and, in so far as the policies of the Bureau allow, approve such plans built upon the local necessities of the states in which they originate.
10. Divorce entirely medical care from hospital care.

After mature consideration and considered judgment the special committee reported to the Executive Board that "from a practical standpoint the direct payment to the physician and hospital is the most feasible under an emergency war program. The committee also reported on the question of "supplemental fees" that it "is of the opinion that pediatricians will willingly and patriotically contribute the differential between usual pediatric fees and those allowed under the EMIC Program;" both of these conclusions, however, carried the reservation that, "The Committee makes it emphatic that these conclusions and recommendations are based solely upon the exigencies of war."

The further recommendation was made that there should be a differential fee between that of the pediatrician and general practitioner and that additional compensation should be provided in cases of severe or prolonged illness.

The complete report of the EMIC Committee together with the report of its acceptance, with certain reservations, by the Executive Board may be read in the July number of the JOURNAL OF PEDIATRICS (**25**: 92-96, 1944).

It is refreshing and encouraging to report to the Academy that the labors of its officers and committeemen and women have met with a considerable degree of success as measured by recent developments. Much of the credit for this desirable outcome should be accorded the endeavors of the special EMIC Committee members, more especially their composure of debatable issues attained through collective interchange of thought at their productive meeting last June.

Upon this occasion, the Associate Chief of the Children's Bureau together with the other members of the committee reached a consonance of opinion, as expressed in their report to the Executive Board, based upon the realities of the actual necessities inherent in a state of war.

Practically all of the recommendations of this report have now been put into effect by the Children's Bureau, which should be credited with

an earnest endeavor to meet the wishes and acquiesce in the proposals advanced by the Academy. In evidence of this mutual concurrence may be cited the new amendments announced in August and September to the state administrative agencies. Complete copies of these changes have been sent to your state chairmen and to the agencies administrating EMIC where they are available for detailed information.

AMENDMENT No. 7—Extends the period of authorization for hospital care of the sick infant to twenty-one days in order to bring it into agreement with the authorization for medical care for a like period.

AMENDMENT No. 8—Provides that the States, if they wish to do so, may adopt differential rates of payment for specialists in obstetrics, pediatrics, and other types of medical service. "Rates of payment for specialists for care confined to their specialty . . . shall not exceed by more than fifty per cent the maximum rates established in EMIC Information Circular No. 1 . . . but in no case shall such rates of payment exceed those customarily received by such specialists." Under this amendment, also, is carried the definition of specialists, to wit: "If differential rates for specialists are established by the state health agency a specialist shall be defined as a physician who is a graduate of a medical school approved (at the time of graduation or subsequent to graduation) by the Council on Medical Education and Hospitals of the American Medical Association and who has been certified by the American Board of his medical specialty or has the training and experience for admission to the examinations of such Board."

AMENDMENT No. 9—Provides that the States, if they so desire, may make individual adjusted payments for the care of exceptional cases (sick infants having long or severe illnesses and nonobstetric intercurrent conditions in maternity patients), because "experience indicates that the majority of infants cared for so far under the program have been suffering from more than the usual minor ailments and that a certain number have required many home or hospital visits within the first week or two." This authorization reads, "A state health agency may make provision under its state EMIC plan for adjusting, on an individual case basis, payments to physicians for extraordinarily severe cases that require an exceptional amount of care by the attending physician within a period of time covered by a single authorization for care of a sick infant or a non-obstetric intercurrent condition in a maternity patient."

AMENDMENT No. 10—Makes it possible for state agencies, if they wish to do so, to offer to physicians office medical care of infants including immunizations, on an annual fee basis. This is an *alternate plan* which may replace, if the physician so desires, the fee for service method now in use. "This office medical service may be provided at rates not to exceed $16.00 a year with appropriate reductions on an equitable basis when the minimum services required by the state agencies have not been provided." "If health supervision, including immunizations,

is provided at a child health conference, the rate for office medical care shall not exceed $10.00 a year."

This amendment would apply largely to general practitioners, especially those caring for a number of infants under the EMIC plan, and has evidently been devised to reduce "paper work" to a minimum. It is doubtful if it would find much usage among pediatricians, but if chosen by them, would carry the provision for a 50 per cent differential in compensation. This annual plan would also not prevent the application of Amendment No. 9 providing for increased compensation for prolonged illness in infants.

AMENDMENT No. 11—Provides that the states, if they desire to do so, may pay for health supervision in physicians' offices and office medical care of sick infants. (The Academy representatives as indicated heretofore, advised the separation of services for the well baby and the sick one.)

"When included in a state plan, this service shall cover complete health supervision, including immunization (as in Section IV,B,4) and office medical care for sick infants. It may be provided at rates not to exceed $24.00 a year with appropriate reductions on an equitable pro rata basis when the minimum services required by the state agencies have not been provided."

This section would carry the differential increase of compensation for qualified pediatricians if qualified as specialists, of 50 per cent as well as the provision for adjustment in case of prolonged illness requiring an excessive number of visits. If embraced by a pediatric specialist, the fee would be $36.00 per year on an annual basis.

This amendment also carried a provision for Public Health Nursing Services, with the following wording, "Provisions for home visits by public health nurses of either public or voluntary agencies shall be included in the plan for infant health services whenever they are available or can be arranged in the community."

SECTION V of this amendment carries this provision as to the qualifications for physicians giving pediatric services to newborn infants and health supervision in physicians' offices. "Diplomates of the American Board of Pediatrics or physicians who have completed at least one year of graduate training in a pediatric residency approved by the Council on Medical Education and Hospitals of the American Medical Association."

"Exception: When a physician has had experience in rendering supervised service in a child health conference that in the opinion of the state agency qualifies him to provide health supervision in his office, he may be designated to provide health supervision in his office even though his training in pediatrics is less than here defined."

Several of the amendments quoted allow the states the option of embracing them in state plans if they wish to do so, but are not compulsory. This policy, adopted by the Bureau, is in keeping with that advocated by

your representatives that the states be permitted greater elasticity in developing their programs to meet their individual needs. Already the chairman of the EMIC Committee has received from a state chairman a communication from one state official declining to put into effect a part of these permissive amendments, which is exactly as it should be, as it gives the state the right to use discrimination and judgment as to its own local needs and abilities to fulfill those needs. In our opinion this is a most healthful sign of decentralization of policy control, and reveals a disposition on the part of the Bureau to permit a greater latitude of state control in the development of its programs, as advocated during the meeting in June of the EMIC Committee. Another request to the Bureau appearing on the agendum of this meeting, namely, the withdrawal from circulation of Folder No. 31, titled, *Maintaining Well-Baby Clinics in Every Community*, has been acceded to and, according to the statement of the Associate Chief of the Bureau in the October number of the JOURNAL (**25**: 365, 1944), "This publication is not now being distributed and will be redrafted to make the position of the Bureau clear before reprints are ordered."

Several of these amendments I have quoted represent distinct gains in light of the Academy's contentions, which have in all instances been advanced upon two basic considerations, (1) that medical service of the highest quality available be afforded the infants of our servicemen, and, (2) that the standards and principles of the science of pediatrics be preserved against hurt or injury, either to itself as the earliest exponent of protection of the health and welfare of children, or to its forward-looking adherents who have never been found wanting in altruism nor in the precepts of benevolence toward those who are underprivileged.

The Executive Board of the Academy at its last meeting pledged its aid and that of the Academy which it represents to the Children's Bureau in support of the EMIC Program.

The Academy has covenanted in its constitution to "perpetuate the history and best traditions of pediatric practice and ethics; and to maintain the dignity and efficiency of pediatric practice in its relationship to public welfare."

The Academy of Pediatrics, which is the descendant and heir of a long line of honored laborers in the field of child welfare, will continue to lend its aid, which is not inconsiderable, and its earnest cooperation, which has been repeatedly sought, to every agency striving for the betterment of child life whose activities are not inconsistent with the constitutional covenants just set forth.

To this end, we of the Academy should, and I am confident do, earnestly "pledge our lives (some part of), our fortunes, and our sacred honor."

November, 1944.

Editorial

THE WARTIME CONFERENCE ON CHILD HEALTH

THE first meeting of the Academy in two years held in St. Louis Nov. 9, 10 and 11, 1944, was not only an outstanding success but also an important meeting from many standpoints. There were 459 Fellows registered, which is a remarkably high figure considering that 355 Fellows are in service with the Armed Forces. In addition there were 13 official guests and 211 registered visitors, including a large group of younger pediatricians who took the board examination held Nov. 8 and 9. Including exhibitors the total registration was 973.

Thursday, the first day, was spent at morning and afternoon clinics at St. Louis hospitals, and in the evening Dr. Alexander T. Martin presided at a Symposium on Rheumatic Fever. The discussion included the clinical and public health aspects of rheumatic fever and the program of the Children's Bureau. The list of speakers will be found in the program published in the December JOURNAL (**25**: 599, 1944) and the papers presented will be published in a subsequent issue of the JOURNAL.

Friday morning was given over to the presentation of scientific papers and the luncheon for state chairmen was held at the noon hour. In the afternoon a discussion of the EMIC program was held with Dr. Joseph H. Wall presiding. At this meeting a report of a special Committee on Consideration of Child Health in the Postwar Period was presented and adopted. This subject was discussed in an editorial in the December JOURNAL (**25**: 639, 1944). The annual dinner that evening was attended by over 600.

Saturday morning was given over to the presentation of scientific papers followed by luncheon groups at noon.

The meeting closed with the annual business session Saturday afternoon. Dr. Joseph S. Wall was inducted as president for 1945 and Dr. Jay I. Durand elected vice-president (president-elect). According to custom the Mead Johnson awards were presented at the business meeting. The first award was given to Dr. Fuller Allbright of Boston and the second to Dr. Joseph Warkany of Cincinnati. For the first time the Borden Award of $1,000 and a gold medal for outstanding achievement in research related to infant nutrition were awarded. The award is administered by and the recipient selected under rules adopted by the Academy. The first recipients were Dr. Henry Gordon and Dr. Samuel

Z. Levine, assistant professor and professor of pediatrics respectively at Cornell University Medical College, in recognition of their metabolic studies in the nutritional requirements of premature and full-term infants. Similar awards to encourage and give recognition to scientific research in the fields related to the food industry given by the Borden Company are administered by six other scientific associations.

The commercial exhibits were numerous, but the scientific exhibits were fewer than usual. This is a phase of the annual meeting which should be developed when peacetimes return.

The Pediatrician and the War

The following Fellows of the American Academy of Pediatrics have been promoted:

Lieutenant Colonel Glen E. Harrison, Mason City, Iowa to Colonel
Major Henry N. Pratt, Boston, Mass. to Lieutenant Colonel
Major Robert P. Rogers, Greenwich, Conn. to Lieutenant Colonel
Lieutenant Thomas S. Weaver, Nashville, Tenn. to Captain

Dr. Francis C. McDonald has entered service as Lieutenant Commander in the Naval Reserve.

News and Notes

Commander Alvin F. Coburn (Medical Corps) United States Naval Reserve, delivered the thirteenth annual series of the Benjamin Knox Rachford Lectureships on Tuesday, Jan. 16, and Wednesday, Jan. 17, 1945, in the auditorium of the Cincinnati Children's Hospital Clinic and Research Building. The subjects of his lectures were "The Rheumatic Problem: Present Status" and "The Rheumatic Problem: Approaches Awaiting Development."

Dr. Maurice L. Blatt of Chicago died Dec. 10, 1944.